

Research Advisory Committee on Gulf War Veterans' Illnesses

September 19-21, 2005 Committee Meeting Minutes

U.S. Department of Veterans Affairs  
810 Vermont Ave, Room 230  
Washington, D.C.



**DEPARTMENT of VETERANS AFFAIRS**

**Research Advisory Committee on Gulf War Veterans' Illnesses  
VA Eastern Kansas Healthcare System (T-GW)  
2200 S.W. Gage Blvd. Topeka, KS 66622**

I hereby certify the following minutes as being an accurate record of what transpired at the September 19-21, 2005, meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses.

---

/signed/

James H. Binns,  
Chairman

Research Advisory Committee on Gulf War Veterans' Illnesses

**Table of Contents**

**Attendance Record..... 6**

**Abbreviations ..... 7**

**Welcome, introductions, and opening remarks..... 12**

**Exposures and Gulf War Illnesses..... 13**

**What Do We Know About Oil Well Fires and the Health of Gulf War Veterans? Overview and Review ..... 14**

**Medical Outcomes of Oil Well Firefighters – Kuwait ..... 14**

**Fuel Combustion Products, Particulates: Exposures and Epidemiologic Findings in Gulf War Veterans ..... 17**

**Particulate Matter and Neurogenic Inflammation...Oxidative Stress-Mediated Toxicity ..... 17**

**Solvent Exposures in the Gulf War ..... 19**

**Fuel Exposures of U.S. Military During the Persian Gulf War ..... 20**

**Possible Role of Hydrocarbon Fuel Exposures on Development of Gulf War Illnesses ..... 20**

**Effect of JP-8 Jet Fuel Exposure on the Immune System and Lungs ..... 21**

**Public Comment – Day 1 ..... 23**

**Additional Exposures of Possible Concern in Relation to the Health of Gulf War Veterans ..... 23**

**Spatial Analysis of 1991 Gulf War Troop Locations in Relationship with Post-War Health Symptom Reports Using GIS Techniques ..... 25**

**Acetylcholinesterase Activity in Gulf War Deployed and Era Veterans: September 2005 Update .. 27**

**Mortality in US Army Gulf War Veterans Possibly Exposed to 1991 Khamisiyah Chemical Munitions Destruction ..... 28**

**Cancer Patterns in Gulf and Non-Gulf Veterans..... 30**

**Highlights of Recently Published Research ..... 32**

**VA Tissue Banking ..... 32**

**Public Comment – Day 2..... 35**

**Report of the Office of Research and Development..... 37**

<b>Gulf War Update.....</b>	<b>40</b>
<b>Preliminary Findings: Reported Unexplained Multisymptom Illness Among Veterans Who Participated in the VA Longitudinal Health Study of Gulf War Era Veterans .....</b>	<b>47</b>
<b>RAC Committee Business .....</b>	<b>49</b>
<b>Public Comment – Day 3.....</b>	<b>50</b>
<b>Appendix A.....</b>	<b>52</b>
<i>Presentation 1 – Lea Steele.....</i>	<i>52</i>
<i>Presentation 2 – Lea Steele.....</i>	<i>59</i>
<i>Presentation 3 – Gary Friedman .....</i>	<i>63</i>
<i>Presentation 4 – Lea Steele.....</i>	<i>85</i>
<i>Presentation 5 – Bellina Veronesi .....</i>	<i>92</i>
<i>Presentation 6 – Lea Steele.....</i>	<i>105</i>
<i>Presentation 7 – Barbara LaClair.....</i>	<i>111</i>
<i>Presentation 8 – Glenn Ritchie.....</i>	<i>120</i>
<i>Presentation 9 – Mark Witten.....</i>	<i>131</i>
<i>Presentation 10 – Lea Steele.....</i>	<i>136</i>
<i>Presentation 11 – Susan Proctor .....</i>	<i>148</i>
<i>Presentation 12 – Mihaela Aslan.....</i>	<i>156</i>
<i>Presentation 13 – Tim Bullman .....</i>	<i>160</i>
<i>Presentation 14 – Paul Levine.....</i>	<i>166</i>
<i>Presentation 15 – Lea Steele.....</i>	<i>170</i>
<i>Presentation 16 – Timothy O’Leary.....</i>	<i>175</i>
<i>Presentation 17 – Joel Kupersmith.....</i>	<i>179</i>
<i>Presentation 18 – William Goldberg .....</i>	<i>185</i>
<i>Presentation 19 - Han Kang .....</i>	<i>190</i>
<i>Presentation 20 – Lea Steele.....</i>	<i>195</i>
<b>Appendix B .....</b>	<b>197</b>
<i>Public Comment 1 – Wesley Crawford.....</i>	<i>197</i>
<i>Public Comment 2 – Kirt Love.....</i>	<i>199</i>
<b>Appendix C .....</b>	<b>201</b>
<i>Document 1 – Overview of FY2005 VA Funding for Gulf War Research .....</i>	<i>201</i>
<i>Document 2 – Gulf War Research Projects FY2005 – by Topic and Period Funded.....</i>	<i>203</i>

**Appendix D**..... **207**  
*September 30, 2005 Letter from Committee to Secretary Nicholson*..... 207

**Attendance Record**

**Members of the Committee**

James H. Binns, Chairman  
Joel Graves  
Robert W. Haley  
Marguerite Knox  
William J. Meggs  
Steve Robinson  
Steve Smithson  
Lea Steele

**Consultant to the Committee**

Jack Melling

**Committee Staff**

Laura Palmer  
Barbara LaClair

**Guest Speakers**

Mihaela Aslan  
Tim Bullman  
Gary Friedman  
William Goldberg  
Han Kang  
Joel Kupersmith  
Paul Levine  
Timothy O'Leary  
Peter Peduzzi  
Susan Proctor  
Glenn Ritchie  
Bellina Veronesi  
Mark Witten

**Abbreviations**

AChE	Acetylcholinesterase
AFIP	U.S. Armed Forces Institute of Pathology
ALS	Amyotrophic Lateral Sclerosis
CFS	Chronic fatigue syndrome
CRADO	Chief Research and Development Officer (VA)
DoD	U.S. Department of Defense
EAS	Environmental Agents Service (VA)
FM	Fibromyalgia
FY	Fiscal year
GAO	U.S. Government Accountability Office
GIS	Geographic Information Systems
G6-PD	Glucose 6-Phosphate Dehydrogenase
GWI	Gulf War illness
GWVIS	Gulf War Veteran Information System (VA)
IOM	Institute of Medicine
IRB	Institutional Review Board
KKMC	King Khalid Military City (Saudia Arabia)
LOI	Letter of Intent
MOD	Ministry of Defence (UK)
MS	Multiple Sclerosis
NCI	National Cancer Institute
NIH	National Institutes of Health
NGWRC	National Gulf War Resource Center
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OPIDN	Organophosphate-induced delayed neurotoxicity
ORD	Office of Research and Development (VA)
OSAGWI	Office of the Special Assistant for Gulf War Illnesses (DoD)
PTSD	Post traumatic stress disorder
RAC-GWVI	Research Advisory Committee on Gulf War Veterans' Illnesses
RFA	Request for Applications
USGS	United States Geological Survey
USACHPPM	U.S. Army Center for Health Promotion and Preventive Medicine
VA	U.S. Department of Veterans Affairs
VHI	Veterans' Health Initiative (VA instructional program for physicians)
VOC	Volatile organic compound
WRIISC	War-Related Illness and Injury Study Center (VA)



**Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses**

U.S. Department of Veterans Affairs  
810 Vermont Ave. N.W. (Room 230) Washington, D.C.

*Agenda*  
*Monday, September 19, 2005*

8:00 – 8:30	Informal gathering, coffee	
8:30 – 8:45	Meeting called to order Welcome, introductions, opening remarks	Mr. Jim Binns, Chairman
8:45 – 9:00	Exposures in relation to Gulf War illnesses: Review of topics covered in 2004-2005	Dr. Lea Steele, RAC-GWVI
9:00 – 9:15	Oil well fires and the health of Gulf War veterans: Overview and remaining questions	Dr. Lea Steele
9:15 – 10:15	Health evaluation of civilian firefighters who capped the 1991 Kuwaiti oil fires	Dr. Gary Friedman, Texas Lung Institute
10:15 – 10:30	Break	
10:30 – 10:45	Exposure to combusted petroleum products and particulates in the Gulf War	Dr. Lea Steele
10:45 – 11:30	Health effects of particulate exposures	Dr. Bellina Veronesi, U.S. Environmental Protection Agency
11:30 – 12:00	Discussion	
12:00 – 1:00	Lunch	
1:00 – 1:30	Exposure to solvents in the Gulf War	Dr. Lea Steele
1:30 – 2:00	Fuel exposures in the Gulf War	Barbara LaClair, RAC-GWVI
2:00 – 2:45	Jet fuel exposure I: Effects on the immune system	Dr. Mark Witten, Univ. of Arizona College of Medicine
2:45 – 3:00	Break	
3:00 – 4:00	Jet fuel exposure II: Neurological and behavioral effects	Dr. Glenn Ritchie, Battelle
4:00 – 4:30	Discussion	
4:30 – 5:00	Public comment period	
5:00	Adjourn for the day	

**Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses**

U.S. Department of Veterans Affairs  
810 Vermont Ave. N.W. (Room 230) Washington, D.C.

*Tuesday, September 20, 2005*

8:00 – 8:30	Informal gathering, coffee	
8:30	Meeting called to order	Mr. Jim Binns, Chairman
8:30 – 9:30	Additional unstudied exposures of possible concern in relation to Gulf War veterans' health	Dr. Lea Steele
9:30 – 10:15	Gulf War illness symptoms in relation to troop location: Use of GIS spatial analysis	Dr. Susan Proctor, VA Boston
10:15 – 10:30	Break	
10:30 – 11:30	Update on VA research evaluating read-through acetylcholinesterase (AChE-R) levels in Gulf War-era veterans	Dr. Mihaela Aslan, VA New Haven
11:30 – 12:00	Discussion	
12:00 – 1:00	Lunch	
1:00 – 1:45	Mortality in Gulf War veterans in relation to modeled proximity to Khamisiyah demolitions	Tim Bullman, VA Washington, DC
1:45 – 2:30	Cancer in Gulf War-era veterans: Information from state cancer registry data	Dr. Paul Levine, George Washington Univ. School of Public Health
2:30 – 2:45	Break	
2:45 – 3:30	Highlights of recently-published research relevant to Gulf War veterans' illnesses	Dr. Lea Steele
3:30 – 4:15	Tissue banking resources and requirements at the Department of Veterans Affairs	Dr. Timothy O'Leary, VA Office of Research and Development
4:15 – 4:30	Discussion	
4:30 – 5:00	Public comment period	
5:00	Adjourn for the day	

**Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses**

U.S. Department of Veterans Affairs  
810 Vermont Ave. N.W. (Room 230) Washington, D.C.

*Wednesday, September 21, 2005*

8:00 – 8:30	Informal gathering, coffee	
8:30	Meeting called to order	Mr. Jim Binns, Chairman
8:30 – 10:00	VA Office of Research and Development update on Gulf War illness-related research activities	Dr. Joel Kupersmith, VA Office of Research and Development
10:00 – 10:30	Committee discussion with Department of Veterans Affairs Secretary James Nicholson	
10:30 – 10:45	Break	
10:45 – 11:30	Preliminary findings on multisymptom illnesses and treatments from VA's Longitudinal Study of Gulf War-era Veterans	Dr. Han Kang VA Washington, DC
11:30 – 12:00	Discussion	
12:00 – 1:00	Lunch	
1:00 – 1:30	Committee business	Mr. Jim Binns Dr. Lea Steele
1:30 – 2:00	Public comment period	
2:00	Adjourn	

Dr. Beatrice Golomb, Committee member, was not able to be present for this meeting. Dr. William Meggs, Committee member, was not able to be present for the September 19, 2005, proceedings.

**Welcome, introductions, and opening remarks**

James H. Binns, Jr., Chairman

Chairman James Binns called the meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses (RAC-GWVI) to order at 8:34 a.m.

Chairman Binns thanked the Committee members, speakers and public for attending the meeting. He introduced Dr. William Goldberg, PhD, the new portfolio manager for Gulf War illnesses research in the Department of Veterans Affairs' (VA) Office of Research and Development (ORD).

Chairman Binns stated that he wished to encourage discussion of the research to be presented, but asked that public comments be held until the scheduled time unless he specially opened the floor to discussion.

Chairman Binns expressed his pleasure that the meeting would include a presentation by and discussion with Dr. Joel Kupersmith, MD, the new Chief Research and Development Officer (CRADO) for VA. He indicated that he also was very pleased that VA Secretary Jim Nicholson would be participating. However, he expressed deep concern about other developments in VA Gulf War illnesses research since the Committee's April 2005 meeting. He stated that VA was lagging far behind in honoring commitments made by former Secretary Principi in November 2004, which were a response to the Committee's 2004 report.

Chairman Binns noted that the treatment development center research funding announcement (RFA), which was the centerpiece of those commitments, was still under review in draft form. He informed the Committee that Drs. Goldberg and Kupersmith were engaged in discussions with Dr. Steele and himself about the matter. He acknowledged that they had inherited a situation where the topic had not been advanced under previous leadership, but noted that it was clear that the treatment development center RFA would not even be issued in Fiscal Year (FY) 2005, let alone awarded and funded.

Chairman Binns next addressed the status of the general Gulf War illnesses RFA. This RFA was issued in April 2005 and proposals were received in June 2005. He noted, however, that the two merit review panels had only recently been named. The first review panel met on Friday, September 16, 2005, and a second panel was scheduled to meet on Friday, September 30, 2005. As with the treatment development center RFA, he noted that these proposals would not be funded in FY2005.

With respect to the review panelist selection process, Chairman Binns found it equally disturbing that the panel for the first merit review session did not contain a single scientist from a list of names suggested by the Committee. He explained that the Committee had prepared and submitted a list of over 50 suggested scientists' names to ORD in February 2005. He pointed out that a major problem in Gulf War illnesses research at VA had been that past review panels had not contained scientists with sufficient expertise in Gulf War illnesses and related areas. He noted that Dr. Steele had recently been appointed to the second review panel, but that the names of the other scientists were not known by the Committee at that time.

Chairman Binns expressed his concern about three of four new Institute of Medicine (IOM) studies initiated by VA in Fall 2004, which only came to public light when the IOM panels convened in Spring 2005. He stated that these studies were not initiated by ORD, but another part of VA, the Environmental Agents Service (EAS), directed by Dr. Mark Brown. He noted that the EAS is responsible for several

other Gulf War illnesses-related functions, including the War-Related Illness and Injury Study Centers (WRIISCs) and the Gulf War Review newsletter.

Chairman Binns stated that the Committee would normally welcome the involvement of IOM and the distinguished scientists and what that they could bring to bear in analyzing Gulf War illnesses research. He noted that it was a Spring 2005 IOM/VA study that identified the increased levels of brain cancer deaths in soldiers exposed to the Khamisiyah plume. He expressed concern, however, that the three new IOM studies were very limited in both the questions to be addressed and the materials eligible for review. He noted that the IOM panels would not consider animal studies, even though they were dealing with many topics that could only be ethically researched in animals. He also noted that federal research efforts had been focused on these animal studies. He stated that these IOM studies appeared to be a step backward to the era when the government was designing research studies for the purpose of suggesting that no problem existed, rather than trying to find answers for the problem. He indicated that he had expressed these concerns to Secretary Nicholson, along with a request for a complete review and reconsideration.

Chairman Binns also expressed concern that no new members had been appointed to the Committee in 2005, nor had sitting members been reappointed at the required time.

Chairman Binns expressed his belief that the work of the Committee continues to be important. He stated that when the official channels were not working, the Committee was there to point out the problems. When new research was not being pursued, the Committee was there to point the way. He noted again that he had expressed these concerns to Secretary Nicholson, in person, the previous week. He indicated that he looked forward to the day when the Committee's relationship with VA staff could be wholly collegial and mutually supportive. He stated that this would be a much more comfortable role, and have a much more productive outcome for ill Gulf War veterans. Meanwhile, he stated that the Committee was fulfilling an important function, and encouraged Committee members to voice their perspectives to VA staff and leadership.

Chairman Binns introduced Dr. Lea Steele, the Committee's Scientific Director.

Before beginning her presentation, Dr. Steele asked that all present use a microphone when they spoke, in the interest of clarity and for recording purposes. She noted that there was a literature table in the back, which contained agendas and selected journal articles pertaining to the day's presentations. She introduced Laura Palmer and Barbara LaClair, Committee staff.

### **Exposures and Gulf War Illnesses**

Lea Steele, PhD  
Scientific Director, RAC-GWVI

Dr. Steele gave an overview of exposures examined by the Committee over the past two years (2004-2005), and outlined the next steps facing the Committee in examining the data, weighing the evidence, and identifying research needs and priorities. ([See Appendix A – Presentation 1.](#))

## **What Do We Know About Oil Well Fires and the Health of Gulf War Veterans? Overview and Review**

Lea Steele, PhD  
Scientific Director, RAC-GWVI

Dr. Steele gave an overview of the information previously considered by the Committee with regards to the 1991 Kuwaiti oil well fires, along with an overview of the epidemiological findings relating these fires to the health conditions of Gulf War veterans. ([See Appendix A – Presentation 2.](#))

Dr. Steele introduced Dr. Gary Friedman, a pulmonologist with the Texas Lung Institute in Houston, TX. Dr. Steele explained that Dr. Friedman had evaluated U.S. civilian firefighters contracted to extinguish the Kuwaiti oil well fires in 1991.

### **Medical Outcomes of Oil Well Firefighters – Kuwait**

Gary Friedman, MD  
Texas Lung Institute, Houston, TX

Dr. Friedman provided the Committee with his observations regarding the health of civilian firefighters sent to the Gulf in 1991. ([See Appendix A – Presentation 3.](#)) (Note: Blank slides contained color field and aerial photos that were not transferable to black and white.)

Dr. Friedman noted that the civilian firefighters did not receive anthrax vaccine, nor were they known to be exposed to neurotoxins, such as sarin. He stated that these firefighters were the closest to a “pure” control cohort available in an uncontrolled setting.

Dr. Robert Haley agreed that the neurological aspects of Gulf War syndrome were not related to oil well fires. He noted, however, that there was some epidemiological evidence showing an increase in veterans being hospitalized for respiratory problems in the year following the war. He asked Dr. Friedman if a possible sequela of the oil well fires might have been obstruction of airways, exacerbation of pre-existing asthma, etc. He also asked whether this cadre of firefighters might have already purged out sensitive individuals through self-selection, removing “the folks who just couldn’t take it,” and whether it was possible that a portion of the troops who weren’t purged prior to deployment might have experienced reactions to oil well fires.

Dr. Friedman acknowledged that there was a natural selection for the “healthy worker” among the civilian firefighters. He stated that individuals with reactive airway disease or asthmatic issues probably wouldn’t be able to survive these working conditions and could not last long in this career field. He also noted that these firefighters had a “fighter pilot” mentality and may not report health problems. With regards to the increased hospitalization for respiratory problems, he stated that there were other possible exposures that could have been responsible, e.g., sand, kerosene, diesel fuel, munitions combustion products, etc. Oil well fire smoke might have contributed to the initial respiratory problems, along with these other exposures. However, he didn’t see the oil well fire smoke causing long-term problems by itself.

Dr. Jack Melling asked whether it was possible to go back to the companies who employed these firefighters to see if they have a significant employee turnover in the first 1-3 years of employment. He stated that if the answer was “no,” then these individuals would not be physiologically atypical. Dr. Friedman stated that this was an excellent idea, and would look into it. He noted that the average experience for the civilian firefighters was ten years, and that he was not aware of any rookie firefighters being deployed. It was noted that this might have resulted in a “superhealthy worker” effect.

Ms. Marguerite Knox asked for confirmation that these firefighters had pulmonary function tests pre- and post-deployment and that the results showed no changes. Dr. Friedman confirmed this. Ms. Knox compared these individuals to smokers who continue to smoke and exhibited no effects. Dr. Friedman noted that these firefighters were in theater for eight months, and that this was a short period of time to see lung function change. He acknowledged that some of these firefighters might have unreported problems now, but additional fire exposures over the intervening years would have to be considered in the equation.

Mr. Steve Robinson asked how many of the civilian firefighters were smokers. Dr. Friedman stated that there was one smoker out of fourteen firefighters in Dr. Etzel's study. He noted, however, that about 30% of the civilian firefighters were smokers.

Mr. Robinson noted, based on evidence presented at a recent conference in New York City, that there appeared to be an effect among Special Forces soldiers, a self-selected group, where they have resilience to Post Traumatic Stress Disorder (PTSD). He pondered whether this was occurring with this group of individuals, who apparently were completely unaffected by the fires. Dr. Friedman stated that none of these men sought medical attention following deployment or filed worker compensation claims. He noted that one company (Adair Company) had been sold in 1994. These workers dispersed, with many moving to another firm (Boots & Coots).

Mr. Robinson asked if Dr. Friedman's recent follow-up had been a verbal discussion with Boots & Coots, or whether he had reviewed medical records. Dr. Friedman stated it was a verbal discussion with the company's safety and health officers. The response, which he believed was candid, was that there were no problems to report. Mr. Robinson asked how the health of these firefighters compared with domestic/residential firefighters. Dr. Friedman replied that there were study cohorts that showed some minor respiratory problems. However, in industrial settings, these problems weren't seen.

Dr. Steele asked whether oil refinery workers exposed to petroleum fires exhibited any symptom-complex health problems. Dr. Friedman stated that, after looking at thousands of these employees, he hadn't seen these problems. However, these examinations were focused on respiratory issues, and the symptoms might have been overlooked before 1992 or 1993. Based upon his observations since then, he didn't believe that this was an issue in this group.

Mr. Robinson agreed that oil well fires did not cause Gulf War illnesses, but may have resulted in respiratory problems in some veterans. He asked Dr. Friedman if he concurred. Dr. Friedman agreed, and noted that some troops deployed into the oil fields could have experienced acute respiratory symptoms.

Dr. Haley asked Dr. Friedman to comment, for the record, on the possible mechanism by which oil well fires, sand, etc., might cause reactive airway disease. Dr. Friedman stated that reactive airway disease was an asthma-like disorder and could result from a single high-level inhalation exposure. He stated that, based on the reports from the Gulf at the time, there didn't appear to be high concentrations of the substances known to cause reactive airway disease.

Dr. Haley asked when the air pollutant monitoring occurred during the Gulf War. Mr. Robinson stated that it began in May 1991. Dr. Haley recalled that previous speakers had presented information that wind patterns had changed significantly between February 1991 and May 1991. Mr. Robinson noted that most of the sampling stations, which were located in Kuwait, were out of the oil well fire smoke plumes. He noted that the investigators believed this was where the majority of troops were located. Mr. Robinson

noted, as Mr. Joel Graves and other veterans had, that there were troops directly within the plumes for extended periods of time.

Mr. Robinson asked if there were any studies that looked at health effects of inhaling sand less than 10 microns in combination with volatile organic compounds (VOCs). Dr. Friedman stated that the RAND report had found 22% of the particulate concentration to be combustion product, with the rest being fine sand. He noted that the health effects of this exposure hadn't been examined in the report.

Chairman Binns asked Dr. Friedman if he had seen patients in his clinical practice with the type of multi-symptom conditions typical of Gulf War illnesses, and whether they had been associated with any particular type of exposures. Dr. Friedman stated that he had seen well-defined, long-term exposures to high levels of solvents or lead cause similar neurotoxic effects in occupational medicine patients.

Dr. Francis O'Donnell, a Department of Defense contractor, asked Dr. Friedman whether environmental sampling had been conducted by the firefighting companies in the areas where their civilian firefighters worked. Dr. Friedman stated that he was not aware of any such sampling.

Dr. Glen Ritchie, a meeting speaker, asked Dr. Friedman the following hypothetical question: What would be the health outcome of placing military personnel with no firefighting experience in this environment (1991 Gulf theater) for 10-12 hours-a-day, 7 day-a-week, for 90 days, with no respirators or protective gear. Dr. Friedman agreed there may be a natural selection among these individuals, and some wouldn't be able to handle the environmental conditions irrespective of the fires. He thought that the oil well fire smoke may just exacerbate the problem for some. Drs. Friedman and Ritchie commented that they personally would have difficulties in this environment. Dr. Ritchie noted that these military personnel already would fall into a "healthy worker" category but that the civilian firefighters represent the healthiest of the healthy, and really did not provide a representative control group. Dr. Friedman noted that studies looking at health risks from Kuwaiti oil well fires made their assessments based on air quality standards set by EPA, which were overly conservative and set to protect the health of infants, children, and the elderly. He observed that, in considering the health effects of oil well fires, it was important to consider both the health of the exposed and the measured levels of exposure. Dr. Steele noted that the measurements were not taken until after the height of the oil well fire exposures. Mr. Robinson added that, in one report, these later measurements had indicated that exposures were similar to those in major U.S. cities, such as New York City.

Ms. Denise Nichols, a Gulf War veteran, commented that an early IOM report had described elevated lead levels among some Gulf War veterans. Dr. Steele stated that these were autopsy results showing elevated lead levels in a small number of veterans

Chairman Binns asked whether there were other examples of studies that could be done to address the question of the health effects of oil well fires. Dr. Steele stated that it would be informative to look at the health status of other groups in the Gulf region at that time. She noted a recently published study regarding the health of Saudi Arabian National Guard members. These researchers had found no increase in hospitalizations, but didn't examine multisymptom illnesses. Dr. Steele stated that were studies looking at hospitalization rates among Kuwaitis in the periods before and after the Gulf War. In addition to these clinical studies, a new study looking at the health and mortality of Kuwaitis was being conducted by the Harvard School of Public Health, with preliminary findings indicating a 20%-30% higher mortality rate among Kuwaitis who remained in the country during the war, compared to those who left the area. She indicated that the investigators were currently assessing what might account for this increase, and that they planned to conduct future studies, which included health of younger Kuwaitis and prevalence of multisymptom illnesses.

Dr. Mark Witten, a meeting speaker, stated that he had conducted, on behalf of the United States Geological Survey (USGS), Type-2 cell culture studies with World Trade Center dust. He stated that they had found differences in the cytokine production of the individual cell cultures. He was waiting for the USGS to reveal which samples were controls. He stated that he had also published research which found firefighters in Arizona (Phoenix and Tucson), following fire recharge visits (usually without their protective gear), exhibited a significant decrease in interleukin 10 production. He agreed that the fires didn't cause health chronic problems, but there might be transient changes in some cell-mediated immune processes. He also agreed that these firefighters represented a "superhealthy" group which could withstand long-term exposure to this type of hazard. Chairman Binns noted that the World Trade Center dust might contain materials that were not present in the Gulf. Dr. Witten acknowledged this and indicated that his presentation later in the day would show that different particulate types/compounds produced different responses in the lung.

Dr. Steele mentioned that other groups who might serve as "pseudo controls" for selected Gulf War exposures would be military personnel from other countries who served in the Gulf War and that these groups would be considered in more detail at the next Committee meeting.

Chairman Binns thanked Dr. Friedman.

The meeting adjourned at 10:09 a.m. for a break.

The meeting reconvened at 10:21 a.m.

#### **Fuel Combustion Products, Particulates: Exposures and Epidemiologic Findings in Gulf War Veterans**

Lea Steele, PhD  
Scientific Director, RAC-GWVI

Dr. Steele gave an overview of the various fuel combustion products and particulates found in the Gulf theater and the epidemiologic findings regarding these exposures in relationship to ill Gulf War veterans. ([See Appendix A - Presentation 4.](#))

#### **Particulate Matter and Neurogenic Inflammation...Oxidative Stress-Mediated Toxicity**

Bellina Veronesi, PhD  
Neurotoxicologist, Neurotoxicology Division, United States Environmental Protection Agency  
Research Triangle Park, NC

Dr. Steele introduced Dr. Veronesi.

Dr. Veronesi gave a presentation concerning the relationship between particulates/environmental exposures and oxidative stress, and how this might pertain to the understanding of Gulf War illnesses. ([See Appendix A - Presentation 5.](#))

Mr. Robinson noted Dr. Veronesi's statement about seeing a blending of neurological disorders in her research. He stated that this also appeared to be the problem with neurodegenerative disorders affecting Gulf War veterans. He stated that their illnesses defied the traditional diagnoses and were considered MS-like, ALS-like, etc. He asked about the timing of brain sample collection, i.e., how soon after death

should samples be collected for the type of studies Dr. Veronesi was doing. Dr. Veronesi stated that her sample animals were not perfused with special fixatives, which worked well, and shipped in formaldehyde, which would not fix the tissue “too much.” She stated that the brains were probably collected no more than 10-15 minutes after death. Mr. Robinson stated that one of the problems in this area of research was the failure to collect substantive evidence, e.g., tissue samples. He stated that several ill Gulf War veterans were interested in donating their brains for research, believing that this would provide evidence relating to overlapping neurodegenerative disorders. Dr. Veronesi stated that collecting clinical information probably would be a better approach. She stated that all of the populations she referred to earlier had cognitive and fine motor skills problems, which “fall out” with Parkinson’s disease. She suspected that all of the neural populations were affected, but for some, motor neurons were specifically affected. She stated that there would be likely a mix within the Gulf War population of individuals affected by neurodegenerative diseases, with some due to service in the Gulf War and other environmental exposures and others due to aging.

Dr. Haley noted that, from a clinical viewpoint, the chronic multisymptom illnesses experienced by Gulf War veterans seem to wax and wane over a period of time. He wondered if this might suggest a periodic brain cytokine/inflammatory exacerbation. He stated that Dr. Veronesi’s study approach was very provocative, and asked her to speculate what type of brain cell injury back in 1991 might produce a long-term illness with periodic swings of cytokine production and inflammatory conditions. Dr. Veronesi stated this was a good question, and that the answer could relate to innate immunity. She stated that in situations where the inflammation was steady and sustained in the periphery, the cytokines being produced could get through the blood-brain barrier, resulting in neuropathology. She indicated that microglia could be pushed “over the edge” so that they were always active and that there were some insults from which the microglia could not recover. She noted that one of the discoveries in Parkinson’s disease research was that activated microglia resulted in scarring twenty years later. She stated that there was neurogenetic information that could be used to explain Gulf War illnesses, including the findings regarding occupational pesticide exposure in farmers and their rates for Parkinson’s disease. Dr. Haley asked Dr. Veronesi what her study approach would be if she had a bank of Gulf War veterans’ brains. She stated that there were histochemical stains to look for microglia scarring.

Dr. Steele asked Dr. Veronesi to speculate about a situation like the Gulf War, where instead of accumulating toxins over time, individuals were exposed to several toxins in a brief time and whether there might be a synergistic effect. Dr. Veronesi pointed out that the vanilloid receptor (VR) could be stimulated by various triggers, including VOCs, acid pH, etc. With so many different types of chemical insults, the common link could be the vanilloid receptor. In addition, she noted that there was a parallel production of free radicals. She stated that this was a mixed bag, and she was sympathetic to the challenges facing Gulf War researchers looking at the situation after the fact. However, researchers should be able to tease out the problems, one agent at a time, since information was known about the pathways involved. She stated that, in combination, the effects could only be exacerbated.

Dr. Haley asked Dr. Veronesi to explain the microglia response process. Dr. Veronesi stated that the microglia released cytokines, along with free radicals which act in its microenvironment. She also noted that microglia were disproportionally distributed in the brain, with most being found in the hippocampus, substantia nigra, and spinal cord. She also noted that free radicals are very damaging, destroying cell membranes, proteins, etc. She stated that her research showed that this type of damage could occur in the brain, initiated years before and perhaps in combination with multiple exposures.

Chairman Binns asked Dr. Veronesi if there were any implications for therapies, other than avoiding further toxic exposures. Dr. Veronesi stated that the individuals could be eating as many anti-oxidants as possible, along with mega-doses of vitamins C and E.

Chairman Binns inquired as to whether organophosphates simply affected the body at the time of exposure, or were stored with continuing effects. Dr. Veronesi stated that OP had long-lasting effects, but much of the current research was focused on cholinesterase inhibition because it was easy to examine. She stated that there was research that suggested organophosphates were retained in the body, but whether organophosphates were retained in the brain was a question for pharmacokinetic researchers.

Chairman Binns asked Dr. Veronesi for her thoughts on future research in this area. She indicated that she hadn't thought about this in detail, but perhaps one should focus on the increased rate of Amyotrophic Lateral Sclerosis (ALS) in young Gulf War veterans.

Chairman Binns opened the discussion for public questions.

Dr. Allen Fienberg, an audience member who is with Intracellular Therapies, Inc., asked two questions: (1) how might other vanilloid receptors play a role in this process, and (2) whether any human genetic association studies had been conducted. Dr. Veronesi stated that the vanilloid receptors were sensitive to very delicate changes in temperature, etc. She stated that the VR1 receptor was very sensitive to acidity. She noted that the process was very complicated, and they had approached it by looking at proton-charge triggers. She stated her research was starting to show that microglia have VR1 receptors and are sensitive to electrostatic charge, creating inflammation. She indicated that her research was focused on VR1 receptors and couldn't respond about the other vanilloid receptors.

Ms. Nichols commented that Gulf War veterans were dying, and that there needed to be a protocol so that families could donate these veterans' brains for research.

Chairman Binns thanked Dr. Veronesi.

The meeting adjourned at 12:20 p.m. for lunch.

The meeting reconvened at 1:20 p.m.

### **Solvent Exposures in the Gulf War**

Lea Steele, PhD

Scientific Director, RAC-GWVI

Dr. Steele gave an overview of solvents exposures during the Gulf War, IOM's review of the possible health effects of these exposures, and the epidemiologic findings pertaining to Gulf War veterans' exposures to these solvents. ([See Appendix A – Presentation 6.](#))

Dr. Melling asked if there was evidence that Gulf War veterans were exposed to more or different solvents than expected in regular military life. Dr. Steele stated that, for the most part, the solvents used were similar to those used in non-deployed areas. However, she noted a couple of exceptions, including CARC paint and decontamination solvents. She also noted that there was the issue of differing effects resulting from solvent exposure when combined with other Gulf War exposures. She stated that JP-8 jet fuel, for example, may affect an individual one way as a single exposure, but affect him or her differently when combined with other exposures.

**Fuel Exposures of U.S. Military During the Persian Gulf War**

Barbara J. LaClair, MHA  
Research Health Scientist, RAC-GWVI

Barbara LaClair gave an overview of the various fuels, including JP-8 jet fuel, used during the Gulf War, the possible health effects of exposure to these fuels, and the epidemiologic findings pertaining to Gulf War veterans' exposures to these fuels. ([See Appendix A – Presentation 7.](#))

**Possible Role of Hydrocarbon Fuel Exposures on Development of Gulf War Illnesses**

Glenn Ritchie, PhD  
Group Leader, CNS Safety Pharmacology  
Battelle, Columbus, OH

Dr. Steele introduced Dr. Ritchie.

Dr. Ritchie gave a presentation on the adverse effects of jet fuel exposures, with a particular focus on effects on the central nervous system. This included information on how repeated hydrocarbon exposures might synergistically increase adverse effects of exposures to other toxicants in contributing to Gulf War illnesses. ([See Appendix A – Presentation 8.](#))

In response to Dr. Ritchie's mention of acute lymphocytic leukemia cases in Fallon, Nevada, Dr. Steele commented that she had received anecdotal reports of three cases of this cancer among Gulf War veterans in one fueling unit. Dr. Ritchie said that a thorough investigation in Kuwait was needed to examine blood cancer prevalence rates, as Kuwaitis had experienced some of the same exposures as Gulf War veterans. Dr. Mark Witten stated that he had learned, through contacts, that there was a large childhood leukemia cluster in Basra, Iraq. Dr. Steele noted, though, that alarms had not been raised thus far concerning increased cancer mortality rates, aside from brain cancer, in Gulf War veterans. Dr. Ritchie noted that the increased cancer rates were being seen in the children, not adults, of Fallon, NV and Sierra Vista, AZ. Dr. Witten stated that a house-to-house survey in Fallon revealed 18 adults, primarily women, with various forms of brain cancer, with three additional cases reported since December 2004. Dr. Steele asked if symptoms were evaluated in populations with these exposures. Dr. Witten stated that there were anecdotal reports that there was an increased rate of autoimmune disease among town residents.

Dr. Ritchie stated that he wasn't implying that JP-8 jet fuel directly induced the health effects seen in Fallon/Sierra Vista. He stated that there was something unique about this environment and specific toxicants that perhaps interacted with JP-8 through the mechanisms discussed in his presentation.

Dr. Melling asked if the fuel usage in the Bosnian campaign was similar that that used in the Gulf War. Dr. Ritchie stated that, to a degree, it was. He stated that, due to different practices and environments, fuels weren't used to heat tents, for cleaning munitions or for sand suppression. He stated, however, that hydrocarbons may have been used for weed control. He noted that there were fewer vehicles and aircrafts as well.

Ms. Nichols asked if birth defects had been reported in Fallon. Dr. Witten stated that he wasn't aware of any increases, but that the focus of the investigation had been on cancers.

The meeting adjourned at 3:05 p.m. for a break.

The meeting reconvened at 3:30 p.m.

**Effect of JP-8 Jet Fuel Exposure on the Immune System and Lungs**

Mark Witten, PhD  
Lung Injury Laboratory  
The University of Arizona College of Medicine, Tucson, AZ

Dr. Steele introduced Dr. Witten.

Dr. Witten provided a presentation on the effects of JP-8 jet fuel on the lungs and immune system (systemic and skin). ([See Appendix A – Presentation 9.](#)) He stated that research in which he was involved was showing that a Substance P analog might be able to “revive” immune cells adversely affected by acute radiation, formalin, respiratory viruses, etc. He indicated that they hoped it could be used as a dermal treatment for toxic exposures.

Dr. Steele asked how what is known about Gulf War illnesses might be integrated with the information presented by Drs. Ritchie, Witten and Veronesi. She noted that whereas jet fuel may be causing an inflammatory response with a dermal exposure, it may be immunosuppressive when inhaled. Dr. Witten commented that the pulmonary macrophages were designed to monitor the health of the lung, and that age was a factor in terms of immune responses in that the elderly and very young were more susceptible to the effects of exposure. He stated that the “take home message” was that age needed to be taken into account.

Dr. Veronesi asked if this Substance P analog was administered in ultra-low doses. Dr. Witten stated it really wasn't. He said that the levels used in the jet fuel studies to show this effect was about a billion times higher than the normal substance P levels in the lungs of rats.

Referring back to Dr. Veronesi's earlier presentation, Ms. Marguerite Knox noted Dr. Veronesi's description of microglia as scavengers and being of the same lineage as macrophages. She asked if microglia could be considered the “quarterback” of brain immunity in the same way as the alveolar pulmonary macrophages described by Dr. Witten for the lung, and whether microglia decrease in numbers with age. Dr. Veronesi stated that CNS microglia proliferate and go into marked neuropathological patterns called microglial scars or clusters. Dr. Witten noted that phagocytic cells had adapted to operate in virtually every major organ system in the body.

Dr. Steele asked about differences between scavenger cell activity in the brain and periphery. Dr. Veronesi replied that the brain normally wouldn't encounter xenobiotic substances. She stated that the brain was traditionally considered an immune-privileged organ, but the current environment was severely challenging human bodies. Dr. Ritchie stated that the microglia increase may be a response to brain damage. Dr. Veronesi stated that microglia also respond to insults themselves. She noted that she was working in isolated and pure immortalized microglia cultures.

Chairman Binns asked Dr. Witten for his suggestions on future research needed in this area. Dr. Witten suggested combination exposure studies, noting that his group had proposed a project to the U.S. Department of Defense (DoD) to study jet fuel, PB, DEET and trace amounts of sarin in controlled animal experiments. He also noted the need to identify a standardized Kuwaiti sand for these experiments. He stated that cell cultures could be used to rapidly screen toxic combinations, and then utilize animal models for those identified as most toxic.

Dr. Haley agreed with Dr. Witten's suggested approach of using cell culture, followed by animal models, and interpreting all of that in light of the epidemiology. He stated that an interesting phenomenon over the last couple of years is the tendency to ignore animal research in trying to answer questions about Gulf

War illnesses. He noted that there was significant toxicological animal research on sarin, pesticides and other agents but that IOM and other panels have taken the position recently to not consider this research in their analyses. Dr. Witten indicated he wasn't sure why they were taking this position. He stated that cell cultures can provide important information, but still leave questions. He said cell culture studies are valuable in keeping costs down and giving information on where more time and resources should be invested. However, without animal models, interactions can't be observed. Animal studies are more "real world."

Dr. Melling wondered if IOM ever talked with their U.S. Department of Food and Drug Administration (FDA) colleagues, who routinely require animal studies as part of the drug approval process. Dr. Haley stated that the IOM generally interprets animal studies along with human studies, but that VA had tied IOM's hands with the mission it gave them with the Gulf War projects.

Chairman Binns asked Dr. Witten if the Substance P analog drug being developed would have a therapeutic effect long after exposure, or only immediately following exposure. Dr. Witten stated that it works best after exposure, versus pre-exposure, but that he couldn't speak as to the timing after-the-fact. He stated that they were looking at whether it could stimulate the immune system. Chairman Binns asked if Dr. Witten had thoughts on directions for therapy in Gulf War veterans. Dr. Witten stated that the key thing was to develop a good standardized animal model, followed by drug screening and human clinical trials.

Ms. Knox asked if the drug might have the potential to reverse immune system damage. Dr. Witten stated that it was a possibility, and this may be due to increasing stem cell numbers. He reiterated that the research process should involve cell culture experiments with standardized toxins, followed by a standardized animal model and screening of potential drug candidates.

Dr. Veronesi stated that she understood OIF/OEF veterans were not developing the same illnesses as Gulf War veterans. She said the question then is what is different. Dr. Steele stated that question is being asked, and noted that problems were being seen in Gulf War veterans by this point after the war. Dr. Haley stated that when Gulf War troops were returning in April, May, and June 1991, veterans were lining up for health examinations, and that Walter Reed's medical consulting service was inundated. He said there were different categories of ill veterans, with one group being completely devastated. He stated that the initial focus for this group was leishmaniasis. He noted horrible medical problems in the current war, with a large number of traumatic injuries, deaths and post traumatic stress disorder (PTSD). He stated, however, that the multisymptom illnesses and cognitive problems did not seem to be developing.

Mr. Robinson noted that 1.4 million troops had served one, two, or three tours in the current Iraq war. Out of these individuals, 300,000 have been deactivated, with 180,000 being seen by the VA and tracked by ICD-9 codes. He stated that although DoD did not have comparative numbers of the discharge diagnosis for comparison with the presenting diagnosis at the VA, VA statistics did not reveal large numbers of veterans with neurological problems. He said that he had met some OIF/OEF veterans with Parkinson's-like tremor, and it was unclear if this was a PTSD reaction or related to Lariam usage. He stated that the illnesses from this war were better understood, and that DoD was doing a better job reducing the pesticide and hydrocarbon exposures. Dr. Haley noted that there also were no weapons of mass destruction (WMD), including nerve agents like sarin.

Mr. Graves stated that now, after reviewing the research related to all key exposures, the focus needed to be narrowed to those exposures which contributed to Gulf War illnesses. Chairman Binns noted that this was Dr. Steele's intention with the Committee's next report.

Chairman Binns thanked Dr. Witten.

### **Public Comment – Day 1**

Chairman Binns opened the floor to public comment.

Ms. Nichols thanked the scientists present for their concern and interest in Gulf War veterans and their illnesses. She suggested an e-mail network of scientists to brainstorm in the same manner as the discussions at this meeting. She stated that blood cancers were being seen among Gulf War veterans in 1993-1994, and that data on these individuals should be collected. With regard to other populations for study, she noted that there has never been a true study with the U.S. Special Forces troops. She stated that veterans suffering from ALS should be followed for location and exposure pattern data. She also suggested that the research which emerged from the Bhopal chemical explosion be examined. She stated that cardiac and thyroid problems were developing in Gulf War veterans. She suggested that veterans be canvassed to find those who weren't being seen by the VA and their reasons for not seeking care there. She suggested that American Red Cross volunteers could help with this effort.

Chairman Binns thanked Dr. Steele for assembling the meeting. He stated there was a tremendous amount of scientific information that had already been uncovered, but because of the lack of time or established relationships, individual scientists were not fully aware of each other's respective work. He stated that meetings like this one created an opportunity to bring together strands of research that shed a great deal of light on the subject.

The meeting adjourned for the day at 4:45 p.m.

The meeting reconvened Tuesday, September 20, 2005, at 8:34 a.m.

### **Additional Exposures of Possible Concern in Relation to the Health of Gulf War Veterans**

Lea Steele, PhD  
Scientific Director, RAC-GWVI

Dr. Steele gave an overview of various Gulf War-related exposures not previously discussed by the Committee, focusing on microwaves/electromagnetic radiation, contaminated food and water, decontamination agents, and chemical agent resistant coating (CARC) paint. ([See Appendix A – Presentation 10.](#))

Dr. Haley asked what the potential sources of microwave/electromagnetic radiation were. Dr. Steele stated that there was little information available about this. For example, she had received reports that some bases in theater were surrounded by microwave towers. Surveys that had asked questions about electromagnetic or microwave exposures had not elaborated further. Mr. Robinson stated that there were high-frequency satellite communication devices, fire finders, portable particle beam devices, high tension power lines, etc.

Mr. Robinson stated that the Office of the Special Assistant for Gulf War Illnesses (OSAGWI) had a database with information from veteran surveys regarding exposures. He stated it would be interesting to see what had been reported by veterans and in what numbers. Dr. Steele noted that some of OSAGWI's lead sheets were on the Internet, which included individuals' reports.

Dr. Haley stated that Dr. Han Kang's national survey was one of the most important and well-designed studies in the entire body of Gulf War veterans' illnesses' research. He noted that Dr. Kang had a risk factor table in his publications, which listed the most important risk factors. He expressed disappointment, however, that Dr. Kang's tables did not include odds ratios. He had calculated the odd ratios himself, finding all elevated with the highest ratio related to nerve gas exposure. He stated that there were eight epidemiologic studies that included a question about nerve gas, and every study showed nerve gas having the highest odds ratio/relative risk. He commented that epidemiologic studies shouldn't rely on unadjusted relative risks because there were many confounding factors. He suggested asking Dr. Kang, who was scheduled to speak the next day, about the risk factor odds ratios.

Dr. Meggs told the Committee that following an outbreak of food poisoning in Barcelona, Spain, there were affected individuals who had persistent problems. He stated that there was a possibility that a person reaches a threshold when it comes to multiple exposures, e.g., sarin and food poisoning, which pushes their inflammatory responses into overdrive. Dr. Haley stated that this was a good point, and suggested that Dr. Kang's data should provide information about the synergy among these risk factors.

Dr. Paul Levine, a meeting speaker who was also a coauthor with Dr. Kang on the study discussed, commented that a subgroup of deployed Gulf War veterans with an identified cluster of neurological symptoms was examined along with two control groups. He stated that they found that a lot of the illnesses and problems relating to these symptoms were due to comorbidities. He stated that there were no consistent differences between the veterans, except for electronystagmography (ENG) results in a few. He stated that Dr. Kang didn't feel that medical history interviews provided sufficiently reliable data for risk factors. He did note that receipt of multiple vaccinations, both in deployed and non-deployed veterans, stood out more than any environmental exposure. Dr. Haley asked if there were calculated odds ratios for the table in Dr. Kang's *Archives of Environmental Health* paper. Dr. Levine stated that he was involved in the clinical study and couldn't speak as to the analysis of the full group.

With respect to decontamination solutions, Dr. Susan Proctor, a meeting speaker, noted that ethylene glycomonomethylether (2ME) was similar to the deicing additives in jet fuel.

With respect to hydraulic fluid, Dr. Haley noted that there was an ongoing debate within the airline industry about hydraulic fluid exposures during flight. He discussed the history of various tri-cresyl phosphate exposures, including the Ginger Jake incident in the American South during the 1920's. Dr. Witten noted that hydraulic fluid exposure was a real problem on Navy submarines, while Dr. Meggs mentioned a recent incident at the Duke Medical Center.

Dr. Veronesi asked if residual delayed neuropathy was observed in individuals exposed to tri-cresyl phosphates. Dr. Haley stated that the Ginger Jake victims were followed for 30 years. He stated that they found that their peripheral neuropathy resolved over a period of six months to a year, but that a central lesion with spastic paralysis remained. With regards to Gulf War veterans, he stated that there was no evidence of either upper or lower motor neuron lesions. He stated that, in the Ginger Jake cases, the peripheral nerve lesion did repair itself, but the central lesion didn't. He speculated that, if there was repetitive low-level organophosphate exposure, a mild central and peripheral neuropathy might develop. However, because the peripheral damage was so mild, it might not have been noticed before it healed, leaving the central neuropathy undetected. Dr. Veronesi stated that she had worked on a project that studied multiple, low-level exposures to organophosphates and found that it helped nerves regenerate. She indicated that they were not sure why this had happened. Dr. Haley asked her what was known about the central neuropathy in these animals. Dr. Veronesi stated that there was damage to the dorsal cord, but the animals didn't show dysfunction. Dr. Haley stated that this might be an area of interest because it is an important parallel to Gulf War illnesses. He noted that there was early speculation that this could be a

mild form of organophosphate-induced delayed neurotoxicity (OPIDN). However, after conducting peripheral nerve conduction studies, he stated there was no evidence that this was the case in Gulf War veterans.

Dr. Steele noted that there was one epidemiologic study (Spencer) that asked about hydraulic fluid exposure, finding an unadjusted elevated odd ratio of 2.45 for chronic multisymptom illness if they reported cleaning hydraulic tanks.

Mr. Robinson noted reports of industrial pollutants, such as hexavalent chromium, at Al Jubayl. He also mentioned the “loud noise event”, where it was postulated to be a patrol boat attack with missiles. Dr. Haley mentioned the supposed Scud missile explosion at Al Jubayl on the night of January 20, 1991. He stated that this happened near the Seabee’s camp. Mr. Robinson stated that the green cloud they reported was assumed to be left-over rocket fuel, not necessarily a chemical warfare agent.

Dr. Steele asked the Committee to think about additional research, if any, that should be pursued in these less documented or less researched areas. She noted that there should have been a cohort study of the 325<sup>th</sup> Maintenance Company following their excessive exposure to CARC paint. Mr. Robinson noted that VA had made a special exception to track the Seabees at Al-Jubayl, but hadn’t with the 325<sup>th</sup>.

**Spatial Analysis of 1991 Gulf War Troop Locations in Relationship with Post-War Health Symptom Reports Using GIS Techniques**

Susan P. Proctor, DSc  
Assistant Director, VA Boston Environmental Hazards Research Center  
Research Associate Professor, Environmental Health, Boston University School of Public Health and Medicine

Dr. Steele introduced Dr. Proctor.

Dr. Proctor gave an overview of her Geographic Information Systems (GIS) research project looking at Gulf War troop locations in relationship to veterans’ post-war health symptom reports. ([See Appendix A – Presentation 11.](#))

Mr. Robinson asked if it was possible to take Dr. Proctor’s data and self-reported information and match it with historic troop movements in determining chronic multisymptom illness occurrence. Dr. Proctor indicated that would be possible but noted that the project didn’t necessarily need to use GIS analyses and could include data on individuals rather than units.

Dr. Haley stated that this was an important study, but that he hadn’t seen it in PubMed. Dr. Proctor replied that she had published it in a GIS journal because she wanted the methodology known and considered. Dr. Haley noted that, based on his research, the 3<sup>rd</sup> week in January 1991 in northern Saudi Arabia was a “hit”, that is an important time and location in the Gulf War. He stated that this was at the same time Czechoslovakian teams detected sarin at King Khalid Military City (KKMC). He asked Dr. Proctor for her thoughts about this time period. Dr. Proctor stated that several things happened during that week. She stated that their group of study subjects was still in urban areas during that time, but none had been in Al-Jubayl.

Dr. Steele asked if there were Scud missiles reported at KKMC area during that time. Ms. Knox, who was stationed at KKMC January-May 1991, stated that 10 Scud missiles were reported going over KKMC. She asked if Dr. Proctor had looked at the correlation between chronic multisymptom illness

patients and VA compensation. Dr. Proctor stated that her study was based on veteran questionnaire responses at one point in time, and then applying the chronic multisymptom illness criteria to categorize them. Ms. Knox asked if there was a way to correlate the identified chronic multisymptom illness patients with VA benefit compensation. Dr. Proctor stated that there was, and that this was part of the Devens' studies. She stated that approximately 30%-40% of the veterans were on the Gulf War registry, and approximately 8%-9% were receiving compensation. Ms. Knox noted that KKMC was within the Khamisiyah plume area.

Dr. Steele asked Dr. Proctor what it meant that she had identified local hot spots but didn't see global clustering. Dr. Proctor stated that their first question, i.e., the global question, was looking at the whole region at a particular time, whereas their second question looked at each of the locations, drew a buffer area around them, and tested whether cases within that area were significantly elevated compared to the area around them. Dr. Steele asked Dr. Proctor if one normally expected clustering in hot spots, but lost the effect when the lens was zoomed out. She wondered if the small cohort size and Bonferroni corrections might have created a "power issue." Dr. Proctor stated that there were sample size issues when using the global approach. Dr. Steele asked if Dr. Proctor had any sense whether there was some nonsignificant indications of clustering. Dr. Proctor stated that, because of all the questions, they focused on the significant clustering.

Dr. Steele asked if Dr. Proctor had considered working with Dr. Kang's survey data to do a similar analysis. Dr. Proctor stated that she hadn't talked with them, but would be interested in doing such a study.

Dr. Proctor stated that her group was now looking at currently deployed soldiers, and had pre- and post-deployment information on over 1,000 personnel. This study includes in-person cognitive testing, location interviews and questionnaires.

She was also working on a retrospective case-control study, which looks at VA patients diagnosed with ALS and Parkinson's disease and whether there is any correlation between their illness and early military/occupational exposures. This study includes about 100 ALS patients, matched with 300 controls, and 400 Parkinson's disease patients, matched with 1200 controls, with a focus on individuals who were diagnosed between the ages of 30-60 years. It includes all eras of veterans and is not limited to Gulf War veterans. She stated that the research team was currently in the process of conducting case record reviews to confirm diagnoses.

Dr. Veronesi asked if the individuals classified as not having ALS or Parkinson's were being separated into an "other" group for nonspecific neurodegenerative conditions. Dr. Proctor stated that they hadn't determined this yet, and were just starting to see what sort of diagnoses they really had. She mentioned that she was also trying to start an occupational study looking at JP-8 jet fuel exposure in Air Force personnel.

Mr. Robinson asked, with regards to her study of the soldiers in the current war, how many individuals were involved and how many were still in Iraq. Dr. Proctor stated that there were about 1500 troops, primarily deployed in the second rotation. She stated that they will have data from comparison veterans who were not deployed, including a group who is now deployed. This group will have two pre-deployment base lines.

Mr. Robinson noted that the VA was tracking the ICD-9 codes and diagnoses of returning veterans from the current war. He asked what her group was seeing in terms of injuries and illnesses and whether they were seeing unknown problems. Dr. Proctor wasn't sure if she could really answer this question because

the post-deployment data was collected 40-45 days following their return. She stated that they were going to be doing a 10-month follow-up in garrison. She stated that, from their general tracking data right now, they were seeing a number of traumatic head injuries.

Dr. Steele asked if they were conducting neurocognitive and symptom assessment at the short-term (40-45 day) follow-up. Dr. Proctor stated that they hadn't analyzed the symptom data, but there didn't seem to be a lot of symptom reporting. She stated that they were still working on the neurocognitive results.

Following up on Dr. Veronesi's question, Dr. Steele asked if Dr. Proctor planned to include those individuals who didn't meet the case definition of ALS or Parkinson's in a "neurodegenerative" group. Dr. Proctor stated that she hadn't thought about doing this, but may now because of the numbers. Dr. Steele stated that many veterans are reporting ALS-like or Parkinson's-like conditions, and it could be important to look at these individuals.

Chairman Binns thanked Dr. Proctor.

The meeting adjourned for a break at 10:39 a.m.

The meeting reconvened at 10:59 a.m.

#### **Acetylcholinesterase Activity in Gulf War Deployed and Era Veterans: September 2005 Update**

Mihaela Aslan, PhD

Associate Director, Clinical Epidemiology Research Center, West Haven VA Medical Center, CT  
Associate Research Scientist, Department of Internal Medicine, Yale University

Dr. Steele introduced Dr. Aslan.

Dr. Aslan provided the Committee with an interim report regarding her group's on-going study of acetylcholinesterase (AChE) and other enzyme levels in ill Gulf War veterans. ([See Appendix A – Presentation 12.](#))

Dr. Meggs stated that the earlier discussions about this study suggested that AChE-R might be a biomarker for Gulf War illnesses, but that the results presented by Dr. Aslan suggested the opposite now. Dr. Haley stated that he wasn't sure this was necessarily the case, and asked to look at the slide with the Gulf War illness Definitions 1 and 2. Discussions, which included Dr. Peter Peduzzi, PhD, occurred as to the "healthy" and "ill" definitions used for GWI cases and noncases. Questions included whether the control group was "pure," that is, whether it included people with multisymptom illnesses or other conditions. Additional discussions focused on the study's original protocol as set by VA and the initial question and hypothesis posed by the Committee. It was noted that Dr. Soreq's initial data suggested that an elevated levels of AChE-R were associated with chronic symptoms following pesticide exposures, and so might be associated with Gulf War illness.

Dr. Veronesi stated that there was abundant literature on how cholinesterase activity reflects cognitive or mood disorders. She noted that serum cholinesterase was tricky to use as a biomarker because it recovers so fast. She stated that measuring AChE activity in the brain was more tedious but would be more valid. She also noted that peripheral activity doesn't measure central activity. Dr. Meggs explained that Dr. Soreq's work had shown that the ratio of AChE and AChE-R was altered following organophosphate exposures, and that was the basis for this study with Gulf War veterans.

Dr. Peduzzi noted that other analyses using these case definitions had been presented by Dr. Concanto previously, and asked why they had raised questions now. Dr. Haley and Dr. Steele indicated that the concerns related to the effect of the case definitions on the control groups had not been clear until Dr. Aslan's presentation. Chairman Binns stressed that the Yale/West Haven researchers were coping with a situation not of their making. He stated that this process began three years ago, when the Committee suggested and asked what was thought to be a simple question, i.e., compare AChE-R levels of ill Gulf War veterans and healthy controls and see if there was a difference. He stated that the concept was taken by VA ORD staff, and "tortured" into the study proposed to Yale/West Haven VA. He stated that he appreciated the work that this group had done, especially with the limited data available.

Dr. Peduzzi asked for direction from the Committee to address its concerns. Dr. Steele stated that she would follow-up with them on these matters.

The meeting adjourned for lunch at 12:03 p.m.

The meeting reconvened at 1:07 p.m.

### **Mortality in US Army Gulf War Veterans Possibly Exposed to 1991 Khamisiyah Chemical Munitions Destruction**

Tim A. Bullman, M.A.

Data Manager, Washington, DC, VA War-Related Injury and Illness Study Center

Mr. Bullman gave an overview of his group's findings relating to mortality rates, particularly due to brain cancer, among Gulf War veterans possibly exposed to sarin gas from the destruction of munitions at Khamisiyah. ([See Appendix A – Presentation 13.](#))

Dr. Meggs inquired about the controversy surrounding the modeling of the Khamisiyah plume. Dr. Melling stated that GAO had reviewed DOD's plume modeling effort, and concluded that even the revised 2000 model was possibly an underestimate due to deficiencies in the modeling process. He stated it was interesting that Mr. Bullman's findings still showed an excess of brain cancers among "the exposed." He stated that one could postulate that the 100,000 troops identified in the DOD model might be the most highly exposed, although not everyone who was exposed. He suggested that future work look at a comparison of in-theater deployed vs. not-in-theater non-deployed. Mr. Bullman stated that this had been done, and they hadn't found an excess in brain cancers.

Mr. Robinson asked if Mr. Bullman had plotted the troop locations in relation to Khamisiyah. Mr. Bullman stated that they hadn't done this, but it was being considered for future research. He stated that they had looked at their military occupations, and there wasn't a difference between the two groups. The vast majority of both groups were support/truck drivers. The only difference seen between the two groups, based on the available data, was one group was considered "exposed" in relation to the Khamisiyah demolitions and the other wasn't.

Mr. Robinson noted Mr. Bullman's comment about there being no previous sarin studies showing a linkage with cancer. He stated that, even if there was a linkage, the IOM would not consider this data because it doesn't look at animal models in Gulf War veterans' studies. He asked if Mr. Bullman knew what the potential exposure was at Khamisiyah. Mr. Bullman stated that their data didn't address this.

Dr. Steele asked if Mr. Bullman had looked at neurological diseases in its review of the data. Mr. Bullman stated that they had and found that the mortalities between the groups were the same, except for brain cancer.

Dr. Haley stated that this was a landmark study, and the researchers should be congratulated for taking it on and following through. He agreed that it was critical in future research to use GIS plotting of these cases to see if there is a pattern. He noted that this information might help to determine, through back tracking, where the plume was. He noted that there also had been a lot of discussion about this paper, and noted the statement that sarin is not a known carcinogen. He asked if this had ever been tested, though. He stated that he had not been able to find a study where animals were exposed to sarin with the intention of following them long enough to detect cancer. He said most sarin studies were focused on immediate effects, mostly cholinesterase inhibition. He noted that this had shifted somewhat with more recent research looking at long-term effects of low-dose exposure. However, he couldn't find anyone who had studied whether sarin was a carcinogen, particularly for brain cancer.

Dr. Steele inquired about the known etiologic agents for the types of tumors identified in this study. Mr. Bullman stated that risk factors for brain cancer included petrochemicals and agrochemicals.

Dr. Melling noted Dr. Henderson's study, which found that low-dose sarin had immunosuppressive effects. He wondered if her observations might be one biologically plausible mechanism for Mr. Bullman's observation. Dr. Haley stated that this was an interesting idea. Dr. Steele stated that Dr. Henderson's group was interested in doing follow-up studies on immunosuppression to see how long it lasted after low-level sarin exposure.

Ms. Knox noted that KKMC was in the initial 1997 cohort considered exposed to the Khamisiyah plume, but removed following the 2000 revision. She stated it will be interesting to see how Mr. Bullman's findings relate to this area.

Dr. Meggs inquired about the UN Special Commission reports of October 1991-May 1998 that were quoted in Mr. Bullman's *American Journal of Public Health* article. Mr. Bullman stated that these were available on the DeploymentLink website.

Dr. Steele asked about using this type of information in conjunction with data from the large national survey of Gulf War-era veterans. Mr. Bullman stated that group working on this project had wanted to look at the health care utilization of veterans after being notified of their potential exposure at Khamisiyah. Dr. Han Kang, a meeting speaker, stated that this study was currently being published. Dr. Steele asked if there was an effort to use these data (from the plume modeling and health survey) to see if there were symptom patterns related to Khamisiyah exposure. Dr. Kang stated that this research was in the process of being published too.

Mr. Robinson asked for clarification with regards to the brain cancer findings of the non-deployed vs. deployed. Mr. Bullman stated that, when looking at all Persian Gulf-era veterans combined, there was no increase in brain cancers compared to nondeployed. Dr. Haley commented that there was an old fallacy in Gulf War illness research of comparing the whole deployed population with the non-deployed population. He stated that the problem was there was only a small percentage of the deployed population affected. When these numbers are combined and compared, effects can be "washed out" or averaged out. He stated a better comparison would be the Khamisiyah exposed group to the whole non-deployed group. He recognized that comparing the deployed Khamisiyah exposed to the deployed non-exposed controlled for other deployment conditions.

Mr. Graves noted that Mr. Bullman's latency analysis divided the nine-year period into three groups. He stated that it would be interesting to capture the next three year period data, creating a 12-year study. Mr. Bullman said that they were continuing to follow this group, and it would be good to do this. Dr. Meggs commented that the follow-up to this study would be very important to see if the increase in brain cancer was or wasn't a statistical aberration.

Dr. Steele asked if they had compared the mean age at death from brain cancer in these veterans with the general population. Mr. Bullman stated that they had, but he didn't have that information with him. He offered to provide the Committee with this information following the meeting.

Chairman Binns opened the discussion for public questions.

Mr. Kirt Love, an audience member and Gulf War veteran, asked Mr. Bullman if they had studied the post-mortems and compiled data on the lung tissue of the veterans with brain cancer. Mr. Bullman stated that they had requested minimal records for review of the diagnosed cancers.

Mr. Love stated this precursor information might show whether these were primary brain cancers. Dr. Meggs stated that histopathology answered this question. He stated that he didn't believe there was one cancer that metastasizes to the brain with the histopathology of a glioblastoma. Mr. Love stated that animals were euthanized before they reached term in these studies, so there were still questions. Dr. Steele noted that Mr. Bullman's group was working with mortality data and hadn't collected tissue samples.

Ms. Nichols suggested comparing this information with the areas in which depleted uranium was used. Mr. Robinson stated that the depleted uranium exposure maps would pretty much cover the same areas as the Khamisiyah plume map, but noted that the depleted uranium maps were even less reliable than the Khamisiyah maps.

Chairman Binns thanked Mr. Bullman.

### **Cancer Patterns in Gulf and Non-Gulf Veterans**

Paul Levine, M.D.  
Research Professor of Epidemiology and Biostatistics  
Clinical Professor of Medicine  
George Washington School of Public Health and Health Services

Dr. Steele introduced Dr. Levine.

Dr. Levine gave an overview of his group's research on the occurrence of cancer, by type, among Gulf War and non-Gulf War veterans using data from state cancer registries. ([See Appendix A – Presentation 14](#). [NOTE: Preliminary analytic results in Dr. Levine's slide presentation are provided for update purposes only. Because these results are preliminary in nature, they are subject to change following additional data analyses.] This research included cancer among veterans in California, Texas, New York, Florida, Illinois, New Jersey, Maryland and Washington, DC.

Dr. Haley suggested that future studies include North Carolina because the largest concentration of Gulf War veterans lives there. This is followed by Texas and California. Dr. Levine indicated that this was planned, and that the first round of analyses had focused on the states with the largest general populations. Dr. Haley suggested merging in the Khamisiyah plume data into this study too. Dr. Levine invited his colleague, Dr. Heather Young, to comment on this. She stated that they had analyzed the Khamisiyah

data in relation to two states, Texas and Illinois, and found no significant associations. She stated that they didn't have this data for all of the study states at the start of the project. However, they have acquired this data and should be able analyze it at some point.

Dr. Haley noted that Dr. Levine's results suggesting an increase in brain cancer in Gulf War veterans correlated with Dr. Kang's and Mr. Bullman's findings. He noted, however, that the increase in testicular cancer might not have been observed in Dr. Kang's mortality study because most of these individuals are successfully treated and live.

Dr. Levine noted that the institutional review board application for the next round of the study had already been distributed. However, he indicated that, if the Committee believed a particular group, e.g., the 325<sup>th</sup> Maintenance Company, needed additional focus, they were willing to include it in future studies.

Dr. Levine noted that when studying cancer clusters, one needed to define the population before looking for individual cancer cases. He stated that the process should not be done in reverse. Dr. Steele thanked Drs. Levine and Young for their earlier assistance consulting with a veteran's physician and herself with regards to an unusual cancer exhibited in this particular veteran. They had been able to look at their data to see how many of these tumors had been reported in the deployed and nondeployed veterans. While they found that more tumors of the type in question had been reported in non-deployed veterans, she stated it had been helpful to the veteran's physician to find out whether there might have been an association with the veteran's deployment.

Ms. Knox thanked Dr. Levine for helping the Committee in its task of making recommendations to the VA and veterans. She stated that she was a medical officer in the National Guard, and knowing that testicular cancer was found at a higher rate indicates that these soldiers should be taught how to do testicular self-examinations.

Ms. Nichols asked why Oklahoma, Mississippi, Alabama, Louisiana and Kansas weren't being considered in this study. She noted that these states had a large number of veterans assigned to tanks and engineering. Dr. Levine stated that they had focused on states with gold or silver rated cancer registries. He stated that it didn't make sense to go after data unless it was of good quality.

Chairman Binns thanked Dr. Levine.

The meeting adjourned for a break at 2:24 p.m.

The meeting reconvened at 2:50 p.m.

### **Highlights of Recently Published Research**

Lea Steele, PhD  
Scientific Director, RAC-GWVI

Dr. Steele gave a brief review of recent Gulf War research, which included epidemiologic studies, health effects studies pertaining to Gulf War-related exposures, and treatment studies for multisymptom illnesses. ([See Appendix A – Presentation 15.](#))

During the discussion of Dr. Eisen's paper and the issue of whether using the case definition of fibromyalgia and chronic fatigue syndrome adequately captured all Gulf War veterans with fatigue and musculoskeletal conditions, Mr. Kirt Love stated that, even though he qualified for a diagnosis of fibromyalgia, it was not listed in his VA medical record and was being ignored. Mr. Graves stated that he had visited his physician after the last Committee meeting, and had been told that he probably had fibromyalgia. However, the physician had no treatment, other than antidepressants, to provide for the condition.

During the discussion of Dr. McDiarmid's paper, Mr. Robinson noted that test methods to detect depleted uranium have been debated extensively. He stated that there was a movement among returning veterans to not have their urine screened by DOD or VA. He noted that several states have passed laws to have their National Guard units use testing laboratories located outside the United States, and were in the process of looking for ways to pay for this screening.

Discussion occurred about the VA's protocol for depleted uranium testing for returning veterans.

### **VA Tissue Banking**

Timothy J. O'Leary, M.D., Ph.D.  
Director, VA Biomedical Laboratory Research and Development Service  
Acting Director, VA Clinical Science Research and Development Service

Dr. Steele introduced Dr. O'Leary.

Dr. O'Leary gave an overview of considerations related to tissue repositories at VA and establishing a Gulf War veterans' tissue bank. ([See Appendix A – Presentation 16.](#))

Dr. Meggs commented that the solution for the Gulf War problem may lie in the remodeling of the brain, and that the answer may lie in the brain pathology. He stated that the only way to answer these types of questions was with autopsy studies. Dr. O'Leary agreed that a banking effort was important, but cautioned that one had think about what studies needed to be done so that the samples were processed in a manner which allowed useful results.

Mr. Robinson asked about the tissues currently possessed by VA for Vietnam and Gulf War veterans, in relationship to their exposures. Dr. O'Leary stated that he didn't have a complete systematic survey of VA tissue banks, but he didn't believe there was a specific VA tissue database aimed at this purpose. He stated that clinical records could be linked to archival specimens. Dr. Steele asked whether these archival specimens could be used considering the identification concerns raised in Dr. O'Leary's presentation. Dr. O'Leary stated that it was theoretically possible, but he wasn't sure about how to specifically approach it.

Dr. Steele asked if blood samples had been collected for the VA's ALS registry, and whether these samples could be used if a researcher had a study question concerning a genetic association with ALS in veterans, even if the veteran was deceased. Dr. Haley noted that the Belmont protocol had a fundamental

distinction between surgical and post-mortem specimens. Dr. O'Leary stated that there were few issues with specimens from deceased individuals under most of laws, except for HIPPA. He noted that these issues and concepts were still being sorted out. He stated that the conclusion of a conference committee, which he recently chaired, was that federal agencies needed to come together and develop a set of tissue banking guidelines which complied with common rules and current statutes. He also noted that genetic studies provide information on both the living and dead, and the general conclusion of the scientific community has been that next of kin consent is required.

Mr. Robinson noted that the VA had blood samples taken before the Gulf War (Task Force Ripper – Marine), but that no studies had been done using them. He asked if these samples were still available, and if so, if the Committee could be provided, mindful of HIPPA requirements, with information as to what samples were on file. He asked if information about the Armed Forces Institute of Pathology (AFIP) samples could be acquired too. Dr. O'Leary stated he didn't know enough about the Task Force Ripper specimen collection to give a meaningful answer. He said that he would be happy to research this matter though. With regard to the AFIP collection, he stated that it contained many types of specimens, but hadn't been collected in any epidemiologically-directed way. He said that DOD would have to speak as to what information it would provide about their collection.

Dr. Steele asked Dr. O'Leary if there was a listing of what tissue samples VA had on file. Dr. O'Leary stated that he was reviewing this information, and was looking at survey data collected in 2002. He stated that he intended to "get his arms around this problem" within the next month.

Chairman Binns noted that Dr. Paul Greengard had commented that "one good brain" could provide much needed information. He acknowledged that there were legal complexities that needed to be addressed. But, without jumping to the concept of a new facility at VA to collect brains from veterans, with long-term financial implications, he stated that there were two questions which needed to be answered. First, he asked if there might be "one good brain" within the current system preserved in a suitable format for study. Second, he asked if there was already a tissue bank, particularly a brain bank, that a Gulf War veteran could be directed to for donation of his/her organs.

Dr O'Leary stated that he believed there might be relevant brain specimens within the VA system. However, he wasn't optimistic that an "ideal" brain would currently be available in the VA system. He stated that ideal brain would be "fresh", i.e., harvested quickly following death after a short period on life support. He indicated that there was a facility at Washington University in St. Louis which did occasional tissue collection in this manner, but it wasn't the most common situation.

Mr. Robinson noted the VA's fourth mission in relation to the larger community and the potential for a chemical and biological weapons attack on U.S. soil. He stated that the VA might be called upon to conduct autopsies to discover different types of bacteriological or chemical warfare agent exposures. He commented that if the VA didn't have those capabilities now, it might need to consider it for homeland security. Dr. O'Leary stated that mass casualties were an important area, and that DOD had the lead on this matter if called upon by Homeland Security. He stated that this type of investigation took a forensics approach rather than a regular clinical approach. He stated that VA had little forensic capabilities. He stated that the forensic pathology community, while small, was aware of these concerns and had evaluated various scenarios.

Chairman Binns commented that the advantage that VA has with respect to this issue is that it is an extremely large HMO with a large number of ill Gulf War veterans. He suggested that VA could use its network to alert its clinicians to invite veteran patients and their families to consider donating their organs. Dr. O'Leary stated that this was an interesting suggestion. While he wasn't in a position to

commit to this course of action, he would be willing to recommend that the Department evaluate such a program. Dr. Steele asked if there was a precedent for this with any other diseases or situations. Dr. O'Leary stated that he wasn't aware of any. Dr. Steele asked if any current tissue collection efforts at VA involved a "SWAT team" approach to collecting samples from around the country. Dr. O'Leary was not aware of this approach being taken by any government or academic organization. He was aware of occasional partnerships between local or regional commercial and private organizations, but wasn't aware of any on a nationwide basis. He noted that there would be logistical concerns with respect to identifying donors and assuring sufficient supplies. He thought this was a possible approach, but was uncertain how it would ultimately work.

Dr. Steele asked if there was a precedent at VA of bringing tissue samples to a central repository from distant outlying regions. Dr. O'Leary stated that the typical situation was a location with a specific clinical program or a second opinion referral center. He stated that these submissions were made in a way where they were fed into a central location that operated synchronistically with the submitting institution.

Dr. Steele asked Dr. O'Leary if he could elaborate on the National Cancer Institute (NCI) collaborative oncology group mentioned in his presentation. He explained that there were many VA medical centers participating in cooperative trial programs with NCI. Most of these study groups maintained tissue banks, which were specific for the diagnosed tissue containing the cancer. These were collected to determine if the patient qualified for the study and were sent to a central coordinating center, which verified the diagnosis and then would bank the tissue. He stated that, while there was an agreement between VA and NCI for these banks, it was not a program with a lot of central management.

Dr. Steele asked whether making tissue samples stored at VA available to non-VA investigators could be a source of financial support for tissue storage expenses at VA. Dr. O'Leary stated that, in general, tissue banks have mixed models of support. They have some form of core support, but may collect fees for specimen preparation costs. He stated that there was no common support model and that the general philosophy was that fees should cover the actual expenses only, with no realized monetary profit from the tissue transfer.

Dr. Kang informed the Committee that CP458, or the National Gulf War Survey Stage 3, collected approximately 1000 blood samples from Gulf War veterans. He stated that these were sent to the Maverick VA Medical Center in Boston, MA. Dr. Steele stated that she knew field investigators who had been interested in accessing this resource, and asked how they might be able to do this. Dr. Kang stated that the investigator would need to join with a VA principal investigator, if they weren't already one, and submit a proposal to the Hines executive committee. Dr. O'Leary explained that Maverick was an epidemiology and clinical trials coordinating center. He stated that if someone does submit a proposal to this group, it would be good for his office to be contacted, too, so it could be responsive to the situation.

Chairman Binns opened the discussion for public questions.

Mr. Love raised the situation of a veteran in Michigan who wished to donate his brain, but that there was no VA funding for the autopsy. He also stated that AFIP was shutting down, and there were plans to build sample vaults at a new location on a military installation. He noted that there was a time lag and problem trying to get a catalog database of these samples before the agency was dissolved. Dr. O'Leary stated that the situation with AFIP was complicated. He stated that any conclusion as to what would happen with the samples was premature. He stated that AFIP was originally placed on the "black list," but the "black list" had been morphing. With respect to the veteran who wished to donate his brain, Dr. O'Leary asked Mr. Love to provide him with more information so that he could explore the issue in more detail. Mr. Love pointed out that there was urgency to this situation, which Dr. O'Leary acknowledged.

Ms. Nichols stated that numerous veterans over the years have contacted her with questions as to how they could donate their organs. She stated that there has been no protocol for 15 years for accepting these donations. She expressed her anger at listening to a theoretical discussion when the focus should be what samples were currently available and what samples could be collected.

Chairman Binns thanked Dr. O'Leary. He commented that he understood and appreciated the complexities of working in government and large institutional medicine. He noted that taking a proactive stance on a matter which appears to a layman to be relatively straight-forward, i.e., establishing a protocol by which veterans could donate brains, would have a large impact on veterans' impressions as to the federal government's efforts in this area. He encouraged and appreciated Dr. O'Leary's willingness to explore this matter.

### **Public Comment – Day 2**

Ms. Venus-Val Hammack, an Army Gulf War veteran, spoke to the Committee. She indicated that she would have limited comments at this time but would be submitting written comments following the meeting. She did note, however, that VA ORD seemed to be responding very slowly to the Committee's requests and suggestions.

Chairman Binns thanked Ms. Hammack.

Ms. Nichols spoke to the Committee. She stated that she was upset after reviewing information about VA ORD's funding of Gulf War research. She stated this wasn't the Committee's fault, and encouraged it to continue "staying on top" of VA ORD. She stated that research funding issues was one thing, but the disruption that happens when VA Secretaries change is another thing. She stated that the Committee needed to issue an annual (2005) report, listing the problems encountered over the past year that had hampered productive efforts. She stressed that the problems raised during the Committee's meetings needed to be made public. She implored the Committee to remember it was established by Gulf War veterans' efforts, and they were counting on it to take the "lead" for them.

Chairman Binns thanked Ms. Nichols.

Mr. Wesley Crawford, an audience member and Navy Gulf War veteran, spoke to the Committee. (Mr. Crawford submitted a two-page summary of his comments. This can be found in [Appendix B – Public Submission 1.](#)) He informed the Committee that he was suffering from a variety of symptoms, discussed the various exposures he experienced in the Gulf War theater, and outlined six specific requests and recommendations. He concluded by saying that veterans were continuing to be told that they don't have this illness even with documentation and proof. This illness is not limited to veterans who were in the desert. He thanked those within VA, independent researchers and the members of the Committee who were working hard to help the veterans with this illness.

Mr. Robinson inquired about Mr. Crawford's specific service. He informed Mr. Crawford that he was eligible to be seen at the War-Related Illness and Injury Study Center (WRIISC), whose office was located on the 6<sup>th</sup> floor of the building. He offered to escort Mr. Crawford up to their office after the meeting so that he could discuss his options with them. Mr. Robinson thanked Mr. Crawford for his comments and asked to speak with him after the meeting. Mr. Robinson explained that he had found out, in his work with John Richardson and others, that individuals with the Glucose 6-Phosphate Dehydrogenase (G6-PD) deficiency should not receive the anthrax vaccine.

Chairman Binns thanked Mr. Crawford for coming to the meeting.

Mr. Kirt Love, with the Desert Storm Battle Registry, addressed the Committee. He provided a presentation showing his research on the Khamisiyah plume modeling, particularly focused on weather data, from March 10, 1991. He indicated that satellite imagery for that date in 2005 contradicted conclusions from DOD's official plume modeling of the Khamisiyah demolitions. His presentation is summarized in [Appendix B – Public Submission 2](#).

Mr. Robinson stated that the Government Accountability Office (GAO) agreed with Mr. Love that DOD's modeling effort was flawed. Mr. Robinson noted that the direction of the sun was incorrect in DOD's first model, and the third model miscalculated the percent strength of sarin located at Khamiyisah. He stated that Mr. Love was documenting these inconsistencies with great pictures.

Mr. Love stated that the U.K. Ministry of Defence (MoD) had also confirmed GAO's findings. He noted that all his information and photographs were taken from government websites. Mr. Robinson stated that the CIA information had been available since April 2002 when it posted its assessment of the demolition operations in Iraq. He stated that the images were only posted recently. Mr. Love stated that, as of February 2005, Iraq was no longer considered a national security threat, which made the images unclassified. He stated that the information was provided online to assist contractors going into Iraq. He stated that there was more information available in the last few months than in the past fifteen years.

Dr. Haley asked whether there was archival data for March 10, 1991. Mr. Love stated that DOD's Deployment Health office knew where this information was stored, but most of it was still classified, although some of it was part of the 1994 Riegle report. He stated that it was subject to release because of the threat level decrease. He stated that he had been submitting Freedom of Information Act requests for five years and had been informed it was classified. Dr. Haley stated it would also be useful to look at the third week of January 1991. Mr. Love stated that he was studying the entire period of time troops were deployed. He stated the problem was getting hold of the data, especially meteorological data from higher elevations.

Chairman Binns said that he found the CIA satellite image of the oil fire plumes on March 11<sup>th</sup> particularly compelling evidence of the direction the wind was blowing at the time of the Khamisiyah demolition, and thanked Mr. Love for bringing this important information to the Committee's attention.

The meeting adjourned for the day at 5:25 p.m.

The meeting reconvened Wednesday, September 21, 2005, at 8:34 a.m.

**Report of the Office of Research and Development**

Joel Kupersmith, MD

Chief Research and Development Officer, Department of Veterans Affairs

Chairman Binns introduced Dr. Kupersmith.

Dr. Kupersmith provided a general overview of VA ORD's program. ([See Appendix A – Presentation 17.](#))

Referencing a comment by Dr. Kupersmith, Mr. Graves stated that the Committee has earned a justifiable reputation for being hypersensitive about PTSD in relation to Gulf War illnesses. He stated, however, that the Committee does not doubt that it exists, but has concerns when PTSD is used as diagnosis for everything. Dr. Kupersmith stated that he understood.

Dr. Melling asked Dr. Kupersmith to clarify how much direction VA ORD was able to give to its researchers with regards to future research focuses. Dr. Kupersmith stated that it was limited. He stated that they could guide the researchers, but that they couldn't force them to do research that they didn't want to do. He stated that VA researchers all have academic appointments in universities. He stated one of the key elements in recruiting the highest quality physicians to VA has been the research program. He stated this is one of the purposes of the research program and that some may believe it is the most important. He indicated that if they started to force individuals to do research they didn't want to do, they would leave the VA. He commented that, as a dean of a medical school, he learned about "herding cats." He stated that clinicians' salaries did not depend on their research but that basic scientists' salaries did depend, in part, on the research program. He stated that a little more guidance could be provided for them.

Ms. Knox stated that she had worked in the VA as both a nurse and a nurse practitioner. She agreed that VA had contributed to medical discovery and knowledge. She encouraged Dr. Kupersmith to think about ways to make the VA more attractive to physicians so they are rewarded for their service. She referenced Dr. Kupersmith's comments about linking clinical records to research efforts. She stated that many Gulf War veterans had left the system because of access problems and are in need of treatment. She stated it was frustrating to meet veterans who were simply looking for help. Dr. Kupersmith stated that they could only deal with the records they had. He stated that 7 million veterans were being seen by the VA, and this was enough to do many types of studies.

Dr. Kupersmith stated that he believed that things had improved with VA physicians' response to ill Gulf War veterans. He agreed that if an individual went to any physician, not just VA physicians, with symptoms that the physician didn't understand or believe, the patient wouldn't get proper care. He commented that physicians needed to learn how to deal with this as a profession. He did note that VA hoped to bring more specialists into the system through increased Congressional funding. He stated that, based on his observations, the VA system had been revolutionized by the electronic records database. He stated that things were changing in the VA, and outside caregivers were looking to the VA for guidance.

Chairman Binns referenced Dr. Kupersmith's presentation comments about how VA research could benefit from the clinical experience. Chairman Binns noted that VA's current clinical guidelines for Gulf War illnesses were still based on theories of stress. He stated that physicians in the field still have the opinion that these were just difficult patients. He stated that the guidelines needed to be reviewed in order

to get better research feedback and more veterans coming back to VA for treatment. Dr. Kupersmith agreed, and stated that guidelines were meant to be revised.

Dr. Meggs noted that some physicians go out and find answers when he or she has a patient with symptoms that can't be explained. He stated that there has been an institutional attitude against these patients and understanding their conditions. He told a story about a discussion with an elder statesman in medicine who studied lupus back when it was a disease that wasn't understood. This physician was told early in his career not to do research in this area, when lupus patients were treated much like Gulf War patients are today. Dr. Meggs stated his belief that Gulf War illness could be figured out, but it would take the right attitude to move in the right direction.

Dr. Kupersmith stated that he was just talking "on the average." He related his experiences dealing with cardiology patients whose conditions were due to metabolic disorders. He stated that these syndromes were very hard to detect, but the patient's pain was real and should be treated as a pain syndrome, even if the disease wasn't fully understood. He acknowledged that there were many patients who "bounced" from physician to physician looking for help and relief.

Ms. Knox agreed with this statement, and asked for Dr. Kupersmith's help to facilitate the care of Gulf War veterans. She referred to Dr. O'Leary's tissue bank presentation. She noted that fifteen years had passed, but there was still no protocol for these veterans to donate their organs. She stated that Dr. O'Leary had referenced being in his job for 18 months and would have to ask what methods were currently available. She stated her hope that Dr. Kupersmith had colleagues to bring into VA ORD who could help get things moving. She stated that in the private sector, it would not be acceptable if an individual could not answer questions about their program after 18 months. Dr. Kupersmith jokingly said that universities didn't work that quickly either, but acknowledged that Ms. Knox had made a good point about tissue banks.

Chairman Binns stated it was depressing that he had to reiterate what he had said at the Committee's first meeting. He had hoped to engender a sense of urgency for research on Gulf War illnesses. He stated that, to some degree, the Committee had slipped into accepting the pace of change that is historic in this area, which was almost none. Veterans want to see someone taking a proactive stance, seeking to solve this problem in a logical way. Chairman Binns encouraged Dr. Kupersmith to put his staff to the position that they needed to solve this problem. Dr. Kupersmith stated that VA ORD couldn't force researchers to do research they didn't want to do. He stated that he needed to figure out ways to encourage them to get involved in this research, but couldn't promise that the research would be done quickly. He noted that the VA was a single entity, and there were many other entities that fund research. He suggested working to get the National Institutes of Health (NIH) interested in this area. He also suggested seeking industry support because it has the largest pool of research funds. While Gulf War veterans aren't a large enough population to garner industry's interest, their diseases (chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, etc.) do affect a much larger population.

Mr. Robinson stated that he appreciated Dr. Kupersmith's academic view on this issue but that it didn't translate into what veterans needed. He noted that Secretary Principi had stood up publicly and announced that Gulf War veterans' illnesses were a real problem. Further, Secretary Principi said research was needed and would be done with designated funds. However, this research has not happened. Mr. Robinson stated that veterans had heard the platitudes of many administrators over the last 5-7 years that he had been involved in this issue. He stated it was time to stop hearing what couldn't be done. Instead, they needed to hear what could be done.

Dr. Kupersmith stated his belief that he hadn't been saying "what couldn't be done." Acknowledging he might be sensitive or just plain tired of hearing "no", Mr. Robinson stated that he heard Dr. Kupersmith to say that VA researchers could not be forced to do this research. Mr. Robinson said that he disagreed, and noted that the Secretary had made the promise that the research would be done. Further, if the VA researchers weren't interested in doing this work and the 5/8<sup>th</sup> rule prevented the work from being done, then we needed to find a way to get it done, including going back to Congress if need be. He stated the way to encourage researchers to do this work was to educate them about the emerging science in this area. He stated that VA clinicians/researchers had no clue about the Committee or the science it is reviewing, nor was VA promoting this information to their clinicians. He said that this "engine" or area of research needed to be restarted after losing a lot of traction and momentum. He noted that this was due to several unfortunate events, some of which might be criminal in nature, i.e., violations of public law. He went on, though, to say that he was encouraged that Dr. Kupersmith was taking over the CRADO position. Dr. Kupersmith expressed his uncertainty at this comment. He stated that he didn't believe he had said this task couldn't be done. He said that if VA researchers were told that they had to do this research, and subsequently left, then veterans would be harmed. He believed that more could be done to educate VA physicians and encourage them to pursue research in this area. He stated that this was currently happening. He noted that the last research funding announcement (RFA) had solicited more and better proposals. He believed the next RFA would do even better. He stated that as a physician he didn't want to "do harm," and didn't want to harm the system. Mr. Robinson stated the military was similar, i.e., in wanting an all-volunteer force. He stated that he didn't want to force VA researchers to do research they didn't want to do. However, if VA clinicians weren't educated about the issues, they would never be interested in doing the research. Dr. Kupersmith agreed that education was important.

Dr. Meggs commented that he kept seeing smoke and mirrors used by administrators and researchers when it came to Gulf War illnesses. He stated that there were a large number of ill veterans, but the system and sometimes the research was designed to exclude them. He hoped that all concerned could get beyond this and quit dismissing these veterans. Dr. Kupersmith agreed that these difficulties were there, and that education was the first step. He noted that there were many conditions that weren't accepted early on by physicians, but later determined to be real. He related a story about the first description of a heart attack in 1911. He stated that most people fell asleep during the presentation with only one question raised during the discussion. He stated that the problem was analogous to other conditions, but that there were also a lot of political and military culture overtones for this issue.

Mr. Steve Smithson asked Dr. Kupersmith how he intended to have ORD encourage and educate clinicians. Dr. Kupersmith stated that they had a number of vehicles, including on-line and telephone options. He stated that none of these had been used to their full potential in this area. Chairman Binns commented that one of the VA officials involved in this process had referred to the Committee's report as "a waste of a lot of trees."

Dr. Haley commented that the last slide in Dr. Kupersmith's presentation was very encouraging. He understood that Dr. Kupersmith believed the objective was to inspire VA scientists to look at this as a disease, analogous to PTSD, and inspire them to find biomarkers and treatments for this disease, which may be one of the biggest new problems facing veterans in our lifetime. He stated that Dr. Kupersmith was the first CRADO to say this. Dr. Haley believed this was a new vision for VA ORD, and if this message could be carried forward to the field along with the Secretary's commitment of research funds, many VA researchers would jump forward to work on this problem. Dr. Kupersmith noted that this was an issue that would interest investigators. Dr. Haley agreed, and commented that it was intellectually challenging.

Ms. Knox stated that it wouldn't be a new day if the VA clinicians/researchers think Gulf War illness was just fibromyalgia, chronic fatigue syndrome, PTSD, etc. She stated it would be a new day if they think it is a brain disease. Dr. Kupersmith agreed, and stated that the point of seeking biomarkers was to provide a scientific basis for research. Dr. Haley stated that the education task may be very simple if ORD sincerely articulates this idea and the funding options to its researchers.

Dr. Melling commented that he personally understood how difficult it could be to change institutional researchers' directions or focus. He agreed that education and motivation was the key. Another key thing was to get the message across that this issue was not going to go away, nor would the direction change when administrations changed. Dr. Kupersmith found this to be an interesting point. He stated that the stability of VA ORD was very important in this matter too.

Chairman Binns reiterated Dr. Haley's point that this is one of the major health problems of veterans of our generation. He stated that the size of the problem is one of the major disconnects between what research shows and what most people within VA believe. He noted that, during an earlier private meeting, Dr. Kupersmith had been impressed by the high incidence of chronic fatigue syndrome (1.6%, which was 40 times greater than normal) among Gulf War veterans. He stated that these were the numbers that VA staff focused on, rather than the epidemiological research showing that 25%-32% of veterans are affected. He stated that Dr. Kang would be giving a presentation later that morning regarding the initial results of his most recent Gulf War veteran study. He stated that Dr. Kang had found: (1) 35% of Gulf veterans have multisymptom illnesses as defined by the study and (2) 10% of the controls met this definition. Thus an excess of 25% of veterans who served in the Gulf War were affected by these conditions. He stated that VA now had its own research that supports a 25% causality rate within that war, which evidenced a huge problem. If VA ORD would simply trumpet this research when it is published, it would change a lot of people's attitudes. Dr. Kupersmith stated that this was a good point, and that VA staff wanted to work on things that were important to treating veterans.

Chairman Binns thanked Dr. Kupersmith.

### **Gulf War Update**

William Goldberg, PhD  
Gulf War Research Portfolio Manager, VA Office of Research and Development

Dr. Goldberg gave an update on the progress of VA ORD's research program for Gulf War illnesses, including funding levels and announcements for FY2005. ([See Appendix A – Presentation 18.](#))

Mr. Graves asked if the Committee would be able to review the projects included in the Gulf War research portfolio. Dr. Goldberg stated that he would be happy to supply the Committee with a list of the current, on-going Gulf War research projects. Dr. Steele stated that this information had been provided to the RAC office and had been distributed to Committee members at the meeting [[See Appendix C.](#)], but that the funding numbers were slightly different from Dr. Goldberg's presentation slides. Dr. Goldberg acknowledged that the funding numbers in his presentation were slightly lower. He explained that 9.3 million dollars had been spent on these projects in FY2005. FY2006 costs would be higher, because some projects started late in FY2005. FY2006 would be the first full year of funding for these projects. Dr. Goldberg noted that it was better to fund projects at the start of the fiscal year because it ensured that projects get started early and work gets done that year. Dr. Goldberg stated that FY2005 RFA-funded projects would start on or after October 1, 2005. He said the number of projects and total monies granted under this RFA depended on the quality and relevance of the proposed studies. He stated that some

proposed projects might be considered tremendous science, but completely irrelevant to Gulf War illnesses, and so would not be funded under this RFA.

Dr. Goldberg stated that two Gulf War initiatives were currently on the table: the Gulf War Treatment Research Center and the reissuance of the Gulf War Merit Review RFA. He stated that ORD had made a commitment to reissue the Gulf War Merit Review RFA for FY2006. He asked the Committee to provide ORD with suggestions on how to fine-tune the RFA announcement, including issues that needed to be specifically addressed. He suggested including a provision for studies similar to Dr. Proctor's GIS research.

Mr. Robinson thanked Dr. Goldberg for the overview of ORD's research funding process and the relevance priority given to planned or proposed research initiatives. He stated that he looked forward to the Committee being more informed and involved in the Gulf War RFA fine-tuning process. He asked Dr. Goldberg for his understanding of the Committee's mandated role as it pertains to proposed research and research directives for Gulf War veterans. Dr. Goldberg stated that he understood the Committee to be a Federal Advisory Committee, tasked with giving advice, and that ORD was to listen to this advice. He stated that the Committee was to look at the current research, speak with scientists, have discussions in a public forum and formulate recommendations which go to the Secretary and the CRADO to help direct policy. Mr. Robinson stated he was asking these questions so veterans in the audience would understand the Committee's relationship with ORD.

Mr. Robinson noted that the Committee had submitted a list of suggested scientists to be considered for the Gulf War Merit Review panels. He asked where this process stood and whether any of these individuals would be serving on the panels. Dr. Goldberg acknowledged that the first panel hadn't included any, but noted that the second panel included four members from the list. He stated that the list had been used in the recruitment process, but many individuals weren't able to participate for a variety of reasons, e.g. not available for a particular date, involved in teaching or current NIH committees, etc. He stated that researchers were matched to proposals within their area of expertise. He stated that the suggested list didn't contain many whose research expertise was on point with the proposals to be reviewed by the first panel. He stated that the second panel would address neurological, cognitive, and neurotoxicology proposals, and thus would include some individuals suggested by the Committee.

Dr. Steele stated that the Committee had previously heard concerns from field investigators about submitting Gulf War illnesses research proposals for review, only to have them reviewed by individuals who had no experience in Gulf War-related illnesses. She stated that, based on her review of the first study section roster, she wasn't familiar with any of the panelists' names being involved in Gulf War research. Dr. Goldberg disagreed and stated that a number of these individuals had been involved in this area of research. He stated that some were clinicians who could provide guidance on proposed treatment studies and that a variety of individuals were appointed to this panel in order to identify good projects. Dr. Steele noted that the whole purpose of having a special Gulf War research study section was to include researchers with familiarity and experience in Gulf War research. She understood the need for broad expertise on these panels, because of the diverse nature of the proposals. However, to meet the intended purpose of the review panel, some of the researchers needed specific expertise in Gulf War illness research. Dr. Goldberg stated that the panel's charter required the panel to review the quality of the science behind the proposals and that the panels were organized to do just this. Chairman Binns noted that the only reason that these new Merit Review panels were created was to give these proposals special attention. Dr. Goldberg agreed, and stated that it pulled the proposals out of the general project mix and gave them a clear and special hearing. He also indicated that scientists on the panel had outstanding credentials and the requisite expertise

Department of Veterans Affairs Secretary Jim Nicholson arrived at the meeting and was welcomed to the proceedings by Chairman Binns.

Secretary Nicholson thanked Chairman Binns for his leadership of the Committee and his dedication and commitment to this cause. He apologized for not being able to meet with the Committee at its April 2005 meeting. He explained that he had been called away due to Pope John Paul II's funeral. He commended the Committee for its work and commitment to exploring every avenue of science in pursuit of answers to questions that continue to evade us. He stated that the first Gulf War may no longer dominate our news, but there was a common thread between it and the current war. He noted that many of today's servicemen and women were probably being exposed to many of the same conditions and health hazards.

Secretary Nicholson stated that it was common sense that there were veterans who were ill as a result of their service in the Gulf War, and these veterans and their families should have no doubts as to whether their government was committed to getting to the bottom of this problem. He noted that VA currently compensated 4,000 Gulf War veterans for undiagnosed illnesses, but acknowledged that number was overshadowed by the legions of veterans who believed that their health was also compromised as a result of their deployment. He acknowledged that they may also believe that the VA is not doing enough to answer their questions. He noted the misshapen body of misinformation, legends, myths and distrust would grow larger as it took longer to provide definitive answers to these questions. He stated that the symptoms and illnesses needed to be accounted for, and there was a great need to understand the long-term health implications associated with veterans' contact with a diverse catalog of naturally-occurring and human-introduced physical and mental threats.

Secretary Nicholson questioned how we could be sure that we were protecting the health of today's Armed Forces if we didn't understand the threats to yesterday's war fighter. He wondered how we could expect today's citizen soldiers to have faith in their government's ability to meet their post-deployment health needs if the government hadn't provided enough evidence that it could take care of yesterday's veterans.

For these reasons, he stressed that the Committee's work was very important. He stated that it was of great concern for those affected, but it also held strategic importance to our country and its defense. He noted that the Committee's frank assessments and communication with him, as well as his team, were extremely important. He stated that there was a need for new, good, on-point research ideas that used the appropriated funds in the best way possible and in line with the goals established. He stressed again how important the Committee's work was in accomplishing this goal, and thanked the Committee for its service.

Chairman Binns asked if Secretary Nicholson had time for a few questions from the Committee. Secretary Nicholson stated he had another engagement, but agreed to take a couple questions. Before doing this, Committee members introduced themselves to the Secretary.

Mr. Robinson personally thanked Secretary Nicholson for taking an interest in this issue, and expressed his regret, but understanding, that they hadn't been able to meet earlier to discuss certain issues. He expressed concern that progress in this area had slid backwards during the administration transition between Secretary Principi and Secretary Nicholson. He stated his concern, which he believed Secretary Nicholson was aware of, that promises made by Secretary Principi for research and funding had not yet been achieved.

Mr. Robinson stated that the Committee, by its authorizing legislation and charter, was supposed to have complete access and be a full partner in anything and everything the VA did in relation to Gulf War

research. He stated that this was not happening. He expressed hope that, under the new leadership of the CRADO and the Gulf War portfolio manager, it would be a new day. However, he noted that some things had happened within the VA, which Secretary Nicholson might not be aware of, that may in fact be violation of public law. He stated that the Committee had been circumvented by individuals within the VA who formed an IOM panel during the transition between administrations, and seemed to take Gulf War issues light years backwards. He thought that these actions might be a violation of the Committee's charter and authorizing public law. He stated his wish to speak with the Secretary about this in more depth at a later time. As a final point, he stated that one of the biggest problems in enticing good scientists and encouraging good research in this area was the VA's failure to promote the Committee's work. He stated that VA staff needed to be educated about the Committee's recommendations. One of the avenues for this type of education was the Veterans' Health Initiative (VHI) series on Gulf War veterans' illnesses, which Mr. Robinson stated was very outdated and contained very old ideas. He concluded by thanking Secretary Nicholson for his leadership and attendance at the Committee's meeting, and expressed his hope that the Committee could fulfill its intended purpose, i.e., provide advice and guidance as a full partner in planning the direction of research for Gulf War veterans.

Ms. Knox thanked Secretary Nicholson for meeting with the Committee. She stated that Secretary Principi's support of Gulf War veterans had been exciting and stimulating. She indicated that she didn't want her comments to be viewed as a complaint, but rather wanted to stress the importance and urgency of Gulf War veterans' concerns. She noted several veterans wished to donate their organs for research, but action to get this program started and protocols established had been difficult. She hoped that some of these broad research ideas would be made available at the patient level. She noted that there would be no one to function in the next war if current veterans did not receive the care they deserve. There would no longer be a voluntary military service. She noted that veterans were seeking health care outside of the VA to get answers to their questions. She hoped that the Committee would have input that is actually implemented in the funding of these new research ideas. She expressed her belief that if VA employees knew that Secretary Nicholson believed that Gulf War veterans' illnesses were a neurological disease, they would be excited about this and not look at the condition as just fibromyalgia or some unknown chemical multisymptom disease. She stressed that veterans wanted answers.

Chairman Binns assured the Secretary that the Committee was not unappreciative of the good work being done at VA. He noted that several distinguished VA researchers had spoken over the course of the past two days. He stated that their findings were important and hopefully would convince any doubters, along with Secretary Nicholson's leadership, that this is an issue worthy of study. He noted that Dr. Han Kang would speak later that morning and that he would present evidence that 25% of deployed Gulf War veterans are ill from chronic multisymptom conditions due to their service in the war. He stressed this was a huge casualty rate, and was a cause worthy of the VA's attention. Secretary Nicholson agreed.

The Committee thanked Secretary Nicholson for his time. Secretary Nicholson left the meeting.

Dr. Goldberg returned to the podium for questions.

Dr. Melling noted that one of Dr. Goldberg's goals was to stimulate more proposals. He indicated that he wasn't sure how VA's phone system worked, but noted that the Government Accountability Office (GAO) sent automatic voice messages from the Director General, addressing all researchers on a particular issue. He found hearing the Director General himself talk about an opportunity or issue sent a very powerful message. If this could be done within VA, he encouraged Dr. Goldberg to do this. Dr. Goldberg stated that the bad news was "if you have seen one VA, you have seen one VA." He went on to explain that the VA's phone system didn't allow him to pick up a phone and send a voice mail to every VA phone. He noted that he had the means to directly communicate with every VA research program.

He stated that this mechanism hadn't been employed sufficiently or as often as it should have been. However, this would change in the future. He acknowledged that ORD was the heart of the VA research program, and was the point of contact between the researchers and Central Office. He noted though that local VA research offices could send messages from their offices to all researchers at their medical centers. This would allow messages to be disseminated in a two-step chain.

Ms. Knox expressed confusion as to why funded projects were being held up because applications were not finished or lacked signatures. She thought once the deadline had passed, "the door had closed." Dr. Goldberg stated that that was true, but there were provisions that allowed a grantee to finalize administrative technicalities and hurdles after the deadline. The grantee just wouldn't get the monies until this compliance work had been finished. He indicated that NIH had a similar provision.

Dr. Haley agreed that bringing a grant application into compliance was a time-consuming process, and related a personal situation where it took 11 months to get DoD grant monies. This was because three institutional review boards (IRBs), including DoD's own IRB, had to review the project. Dr. Haley stated this type of delay was a problem, but it was a known problem. He stated that the real problem was acknowledging that Gulf War illnesses research was a legitimate area of study. He indicated that there was contempt towards this type of study. Leadership in ORD needed to create a vision among its researchers that this is an intellectually stimulating area of research and this would be where the "game was won." As for compliance issues and delays, Dr. Haley indicated these were not a real problem.

Dr. Haley stated that the other major problem, or stop-gap, in this area of research had been the peer-review grant committees. Before the Gulf War Merit Review Panel, Gulf War illnesses proposals were being reviewed by general medical committees, e.g., gastroenterology, etc. If the members of these peer-review committees knew nothing about Gulf War illnesses, they were not likely to fund studies in this area.

Chairman Binns noted that the meeting was running late, and that Dr. Kupersmith had another meeting to attend. Chairman Binns and the Committee thanked Dr. Kupersmith for speaking with the Committee that morning.

Dr. Goldberg expressed his understanding as to the frustration and disruption that accompanies constant high-level administration turnover. Dr. Steele noted that it was disruptive to progress as well.

Commenting on an earlier point made by Dr. Goldberg, Dr. Steele agreed that RFAs needed to be more focused, with specific questions of interest being posed. She noted that, in earlier RFAs, the Committee had advised that this needed to be done. She stated that she was glad to hear that this is what Dr. Goldberg wanted to do with future RFAs. She was even more pleased to hear that Dr. Goldberg would speak with specific researchers to encourage them to investigate specific issues related to their expertise. Dr. Goldberg indicated that he could notify researchers of these opportunities.

Dr. Goldberg commented that NIH funding rates were decreasing, and many researchers were not pursuing these grants due to the low odds of being funded. He stated the funding rate for Gulf War proposals were historically higher than other areas of research at VA. The funding rate for the FY2004 RFA was 28.6% but that other review panels were funding at a rate of 22%, and as such Gulf War illnesses would become attractive to researchers. Dr. Steele appreciated that the proportion of funded Gulf War illnesses studies had started to go up in FY2004.

Dr. Steele noted Dr. Goldberg's commitment to review the research portfolio to determine if all included projects were really relevant to Gulf War illnesses. She stated that the Committee had reviewed the

funding for FY2005, and that many of the projects identified did not appear to be specific to Gulf War illnesses. (See Appendix C.) She asked Dr. Goldberg if he had thought about the process he would use to determine whether these projects were relevant or not. Dr. Goldberg stated that he would start by pulling the abstracts for every project. Dr. Steele asked if he had thought about the criteria that would be used to make determinations of relevance. Dr. Haley indicated that the Committee could advise Dr. Goldberg about the questions that needed to be answered, along with how to detect non-relevant research disguised as Gulf War illnesses research. Mr. Robinson stated that this was his understanding of what the Committee was supposed to be doing. In other words, the Committee would have some knowledge of the proposals and be able to give an opinion, not make decisions, about research proposals.

Chairman Binns stated that the sad aspect of the FY2004 RFA funding story was that, while there were a higher number of projects funded, over half were related to stress-based theories. He stated that was why the FY2005 RFA specifically excluded these types of studies. He noted that the Committee had heard presentations on some of the funded proposals at the East Orange, NJ, War-Related Illness and Injury Center, and had found some of them “fanciful” at the time. He stated that 28% was a good funding rate, but it didn’t necessarily satisfy the quality or relevance elements.

Chairman Binns appreciated and sympathized with Drs. Kupersmith’s and Goldberg’s position of taking over a situation where there has been lots of turnover and lack of staff. However, there had been an Acting CRADO and other officials who held these offices since Secretary Principi and Chairman Binns stood in that room before the press and public and committed to spending up to 15 million dollars in new FY2005 research. He noted that FY2005 was basically over, and projects funded under the FY2005 Gulf War illness RFA had not been awarded yet, nor had the treatment research center RFA been announced. He did not fault Drs. Kupersmith or Goldberg, but predecessors in their positions had been aware of the commitments made and these commitments have been totally unmet. He stated his concern that this “lost” year was being allowed to be lost, and that there would be no effort to make up for lost time. He stated that proposals submitted under the FY2005 RFA wouldn’t be funded until 2006, and the FY2006 proposals wouldn’t be funded until 2007. Dr. Goldberg stated that this was a typical time schedule for processing an RFA. Chairman Binns again stressed that a year had passed, and nothing was in place to meet or catch up to research funding commitments that had been made.

Dr. Steele noted that there needed to be assurances that this slow action would not continue. Dr. Haley stated this raised the question as to whether the FY2006 procurements could be more expeditiously done so they were awarded in FY2006. Dr. Goldberg stated that the plan was to get the treatment research center RFA out as quickly as possible, with the intention of getting those started in FY2006. This was his first priority, followed by the FY2006 RFA. He stated that they would not be artificially delaying the submission date for the FY2006 RFA or the timing of the review to force funding in FY2007.

Dr. Haley suggested that, if the ORD office was understaffed, the Committee might need to make a recommendation to the Secretary that additional staff be hired to get this job done. He stressed this was the greatest health threat to veterans to have occurred in recent times, and that it needed to be addressed. If additional staff was needed to handle the workload, the Committee needed to advise that more staff be hired.

Ms. Knox stated that the Committee needed to help devise solutions to getting more research proposals. Dr. Goldberg stated that better communications should dramatically increase the number of submissions. Ms. Knox asked Dr. Goldberg about the communication methods he would be using. Dr. Haley stressed that it wasn’t just communicating that there is an RFA, but also the vision of what needed to be done. Dr. Goldberg stated that the first step was to communicate with the research offices of the 70-odd medical

centers with active research programs. He hoped that the RFA would also give much better guidance on the type of research needed.

Mr. Robinson stressed that Dr. Goldberg should become involved in the VHI series, because this is the document to which VA clinicians and researchers refer for treatment options and information on the status of Gulf War veterans' illnesses. He noted that the current guidelines are 10 years out-of-date.

Dr. Melling suggested that a letter go out from Secretary Nicholson to the VA research community, in which the Secretary stressed the importance of this research. Mr. Smithson noted that Secretary Principi had made a video in a previous year, attempting to change this attitude and encourage researchers to apply for these grants. He asked if ORD had sent this out to the VA research community. Dr. Goldberg stated that he couldn't answer this, but felt it was probably in the same category as the RFA. If someone wants to look at it, it is there. He stated it hadn't shown up as an e-mail attachment to every VA researcher. He stated that the system, up to this date, had been quite passive, and that it was his responsibility, as the new portfolio manager, to make the communications more active. Ms. Knox stated she liked this attitude. Dr. Haley commented that he thought this video had made some rounds among researchers. With better RFAs and Dr. Kupersmith talking about biomarkers, etc., he felt this would do the most to encourage good proposals.

Chairman Binns noted that this was the same problem faced by the Committee. The Secretary of the Department of Veterans Affairs had put together a video showing that he was completely behind Gulf War illnesses research, and it was sent out to the field. So, the VA research community had heard this message before. He noted that, at the same time, when a VA researcher called ORD and asked if special attention was going to be paid to Gulf War illness proposals under the Deployment Health RFA, he would be told by the then portfolio manager that no special consideration would be given these proposals. He stated that, if the Committee was going to tell veterans that progress was being made, there needed to be action to back up these statements. He went on to say that, even if there was a new video made by Secretary Nicholson, its effect had already been diluted because of the failure in the past enforcement of this message. He stressed that, at this point, the only thing people would believe would be action. Dr. Goldberg stated that he couldn't argue with this.

Dr. Goldberg stated that he had looked at the FY2005 funded project list, along with the proposed FY2005 projects. He believed that the quality, relevance and types of projects submitted in FY2005 were much better. He thought researchers understood how important this research was by ORD simply issuing the RFA a second time. He believed researchers would realize that ORD was really serious about this research when the RFA was released the third time. He didn't want to say that researchers were mercenaries, but they would follow the money in the long run. He noted that researchers' focuses change or evolve over time, and they will apply their knowledge and techniques to new areas in order to maintain their sanity and the health of their laboratory. He cautioned that this change wouldn't happen overnight, but it would happen. It was his job to make sure that path was there, visible and unimpeded. He commented that "if you build it, they will come." Mr. Smithson noted that Dr. Goldberg also had to let them know that it was being "built."

Chairman Binns invited public questions.

Ms. Nichols suggested the following to Dr. Goldberg: (1) VA sponsor a conference on Gulf War Illnesses. She stated it had been almost four and half years since the last conference, and it might trigger some new research; (2) VA research publications should announce these RFAs and review what had been learned; and (3) the Committee should be utilized to get this information out to the researchers. She

suggested having Drs. Steele or Golomb do a segment for the VA's television network on these matters, in an effort to start a dialogue between researchers, the Committee and ORD.

Ms. Hammack suggested that VA's Public Affairs office be utilized to get this message disseminated. She noted that printed media, not just electronic media, needed to be utilized. She listed two printed periodicals, VA Guardian and US Health, as being possible target publications.

Ms. Hammack asked Dr. Goldberg if he interacted with Dr. Mark Brown and the Deployment Health Working Group. Dr. Goldberg stated that, as the Gulf War Illnesses Research Portfolio Manager, he had a position on the research subcommittee and was responsible for putting together its next report to the Congress.

Chairman Binns asked what responsibilities the Deployment Health Working Group had that didn't include Dr. Goldberg. Dr. Goldberg stated that many of the discussions dealt with seamless transition and were focused on issues affecting the current deployment. Dr. Steele asked if there was only one VA representative on the main committee. Dr. Goldberg stated that there were a number of VA representatives, including Drs. Mark Brown, Craig Hyams, and Susan Mather. There were also DoD representatives and a liaison from MoD.

Chairman Binns thanked Dr. Goldberg.

The meeting adjourned for a break at 11:05 a.m.

The meeting reconvened at 11:23 a.m.

**Preliminary Findings: Reported Unexplained Multisymptom Illness Among Veterans Who Participated in the VA Longitudinal Health Study of Gulf War Era Veterans**

Dr. Han Kang, DrPH  
Director, Washington, DC, War-Related Illness and Injury Study Center  
Environmental Epidemiology Service, Department of Veterans Affairs

Chairman Binns introduced Dr. Kang. He noted that Dr. Kang was the first researcher within VA to step forth and take the kind of proactive effort that the Committee had been encouraging this morning. Dr. Kang had a study that was well underway, with the questionnaire already sent for OMB approval and printing. He volunteered to bring it back, found ways to finance the additional costs, and included several pages of questions recommended by the Committee. The Committee commended and thanked Dr. Kang for his work.

Dr. Kang gave an overview of his group's preliminary findings with respect to unexplained multisymptom illness among Gulf War veterans and the effects of various practices and treatments on their symptoms. ([See Appendix A – Presentation 19.](#)) He explained that the data analysis in this study was complex because the questionnaire responses relating to treatments were open-ended and handwritten, not the pre-structured, machine-readable responses that are typically used.

Mr. Graves asked if any of the era veterans received vaccinations, but weren't deployed. Dr. Kang stated that this was addressed earlier in the study. Discussion occurred as to whether there were vaccinated veterans who didn't deploy. Mr. Smithson commented that DoD's position was that there was a very small percentage of non-deployed, vaccinated veterans, because most were vaccinated in theater. Mr. Graves stated that his unit received their vaccinations before deployment, and there were individuals who

didn't deploy. He noted this was significant and these veterans needed to be identified because it might explain why some of the era veterans has multisymptom illnesses.

Mr. Graves also asked if the questionnaire included questions about whether cost affected veterans' choice of treatment or therapy. Dr. Kang stated this question was not asked. Mr. Graves noted that the high over-the-counter drug usage might be explained by their lower cost compared to the other listed therapies.

Dr. Melling asked whether there was any indication that era veterans had symptoms that began before 1991, and then rolled over into the first part of the study. He stated this might explain the higher numbers immediately following the war. Dr. Kang stated that they had this information from an earlier part of the survey, and could pull this information out for review. Dr. Haley stated this was a very good point, and may indicate that there is a different profile in the deployed and non-deployed with respect to pre-existing symptoms.

Dr. Haley commended Dr. Kang on this study. He stated that this was a tremendous survey, and noted that this was one of the first Committee objectives to be recognized by a VA researcher. With respect to future, more in-depth analyses, he suggested pulling out the information on the people who got "well" and "better" versus those who believed they hadn't gotten better. He stated this might help identify treatments that provide veterans with long-term benefits, and help the Committee guide the VA with respect to clinical research trials. He stated this might be the "ultimate fishing expedition" with the hope of finding a useful treatment. Dr. Steele reiterated that this study was a great contribution to Gulf War illnesses research. She noted the contribution was even more than the Committee might realize, because of the difficulty of analyzing open-ended questions on the large sample.

Mr. Robinson commented that these findings were relevant to previous studies regarding cognitive behavioral therapy. He asked Dr. Kang if this survey asked veterans whether they were VA patients or had sought treatment outside the VA. He noted that some of the treatments listed from the survey are not provided by VA. Dr. Kang stated that this information could be acquired because the survey participants could be matched with the VA's treatment database.

With respect to Gulf War veterans finding benefit from drug therapy, Mr. Robinson noted it was interesting to see "illegal drugs" listed as a treatment. He stated that the use of opiates could mask pain, which may be beneficial, but it didn't cure the underlying condition. He stated that he knew several Gulf War veterans who used marijuana, alcohol, etc., because they couldn't get opiates in the VA healthcare system. Their use of these drugs may provide them with a way to survive another day.

Mr. Wesley commented that opiates hadn't helped his condition or pain. He stated it simply provided him with a drug-induced "high", which prompted him to discontinue taking it.

Ms. Knox suggested that the Committee ask the Secretary about mechanisms available to reward researchers, such as Dr. Kang, who have made ground-breaking contributions to Gulf War veterans' research. Chairman Binns indicated that there might be a way the Committee could establish a certificate of appreciation.

The meeting adjourned for a break at 12:07 p.m.

The meeting reconvened at 12:20 p.m.

**RAC Committee Business**

Lea Steele, PhD  
Scientific Director, RAC-GWVI

Dr. Steele outlined proposed plans for upcoming Committee meetings and reports. ([See Appendix A – Presentation 20.](#))

Dr. Haley suggested the Committee address the occurrence of psychological symptoms and states that accompany brain disease. He noted that a high percentage of really ill Gulf War veterans have depression. He noted that a couple of studies show that there is a slight excess prevalence of mania in Gulf War veterans. He believes this had fueled the premise that Gulf War illness is a psychological disease. He noted, however, that 80% of individuals with Multiple Sclerosis (MS) develop depression, compared with 5-10% of individuals who don't have a neurological disease. He commented that no one believes depression causes MS. Psychological symptoms are more likely to appear when certain parts of the brain are affected. Dr. Steele agreed and stated that the point was made in the Committee's 2004 report. She noted this connection was especially pronounced in individuals with toxin-induced encephalopathies.

Ms. Knox commented that a new drug, Cymbalta, treated both depression and diabetic peripheral neuropathic pain. She noted that if there wasn't enough norepinephrine or serotonin within the prefrontal cortex, the individual lacked the neurotransmitters that go to the basal ganglia. This was why the drug could be used for dual purposes. She stressed this drug treated a brain disease, with neurotransmitters lacking in the brain causing depression, and in the periphery causing pain. She stated that the two conditions could not be separated. Dr. Steele agreed and stated that the bottom line was that having psychological symptoms did not imply psychiatric etiology.

Dr. Melling commented that the Committee had looked at a wide range of possible causes for Gulf War illnesses. He commented that this field of research had been "bedeviled" because the illness was multisymptom with a multi-exposure trigger. He suggested that the Committee was in a unique position to weigh the various factors. Dr. Steele agreed and commented that previous review groups hadn't tried to weigh the strengths and weaknesses of the evidence for various exposures contributing to these conditions.

Chairman Binns stated that he was sympathetic to this approach. He noted that one of the comments/criticisms of the Committee's 2004 report was that it was unwieldy with the number of recommendations made. He indicated that the Committee needed to focus on those areas that were most promising, and resist the temptation to improve every area.

Dr. Melling noted that the Committee was short two members. If the Committee did go through this exercise, he suggested that there be a couple new people at the table who could challenge the discussion by asking difficult questions. Chairman Binns agreed. He stated that recommendations for three new appointments had been submitted to the Secretary in Spring 2005. The process had not been completed for a variety of reason. He hoped that these appointments would be completed promptly and before January 2006, which is when the next round of appointments are due to expire. He stated that the Secretary was aware of the importance of this issue. He also agreed that the Committee could benefit from individuals with in-depth scientific expertise in the key areas, while maintaining the Committee's mix of veteran and layman input.

Mr. Graves asked Chairman Binns for his opinion as to why the new Committee appointments had been delayed. Chairman Binns stated that he had been hoping that there might be action before this meeting,

and had some individuals holding these dates in their schedules. He indicated that he did not know and thought it might not be useful to speculate on why it was taking longer. He agreed, though, that there needed to be a full Committee with people who have strong scientific backgrounds in the areas of interest and a view that Gulf War illness was a real problem, which needed to be solved quickly.

Mr. Robinson commented that veterans might not be aware of Chairman Binns' routine communication with the Secretary about the concerns of the Committee. He asked if the Committee should prepare an official document outlining these concerns for the Secretary. Mr. Graves stated that the Committee had sent such a letter to former Secretary Principi. Chairman Binns stated that he had no problem with doing this. He noted that the Secretary was aware of many of these concerns, but there was strength in a letter from the entire Committee. Ms. Knox commented that it was also important to note the VA's positive accomplishments in this area. Mr. Graves stated that a report to the Secretary would be a start to doing this. [Note: A letter from the committee was submitted to Secretary Nicholson on September 30, 2005. [See Appendix D.](#)]

Chairman Binns thanked Dr. Steele and the Committee staff for doing a fantastic job in coordinating the meeting. Mr. Robinson commented that the Committee's first certificate of appreciation should go to them. Chairman Binns noted that, in addition to work outlined in her last presentation, Dr. Steele was working in other capacities, e.g., working with Dr. Goldberg on the implementation of the treatment research center RFA, etc. He stated that he hoped, once VA was producing first-class Gulf War RFAs on its own, the Committee's time could be spent fully on looking at new research opportunities. Dr. Steele said Chairman Binns was kind to point out the work of the Committee staff. She commented that Committee members might not be aware of the time and extensive efforts devoted by Chairman Binns on behalf of the Committee's work. Chairman Binns stated that, hopefully, everyone soon could applaud the real mission of the Committee, i.e., making a difference in the health of Gulf War veterans. He appreciated Dr. Kang's presentation, and thought it was a good note on which to end the meeting.

Mr. Graves noted that veterans in the audience should also be commended for their time and commitment to this issue.

### **Public Comment – Day 3**

Ms. Hammack spoke to the Committee. She asked if the Committee could investigate why Gulf War veterans were being told they couldn't donate blood today. She wanted to know why this policy was still in existence. Mr. Robinson stated that he was not aware of any current Red Cross, DoD, or VA regulation that prohibited these donations. He stated he would be willing to assist any veteran in finding out why they were being denied the opportunity to donate blood. He noted that when troops returned home in the early 1990s, they couldn't donate blood because of concerns about leishmaniasis and certain medications taken in theater. However, time has passed, and these concerns have diminished. Ms. Hammack stated that she had been to a U.S. Food and Drug Administration meeting in 2003, and they were proposing to continue the blood donation ban for Gulf War veterans because of leishmaniasis. Mr. Robinson stated that there is a two-year ban on blood donations for currently deployed military personnel, but not 1990-1991 Gulf War veterans.

Ms. Hammack stated that more information was needed about VA cooperative studies. She stated that the titles of these projects were known, but needed the Committee to recommend that VA clarify, implement, or create a policy that allows veterans to volunteer for these studies. Lastly, Ms. Hammack asked that the Committee make recommendations in its next report regarding the need for a VA Gulf War tissue bank.

Ms. Nichols spoke to the Committee. She thanked the Committee for listening to the veterans and allowing their input at meetings. She suggested that the Committee recommend merit review awards and promotions to reward outstanding VA researchers. She had hoped to learn about the proposals reviewed at the last Gulf War merit review panel at this meeting. Dr. Steele stated this information would be available after the studies were approved. Drs. Steele and Goldberg explained that the proposals were still being reviewed and wouldn't be approved until the second panel had met. Ms. Nichols asked for more specific information about the proposed treatment center. Dr. Steele explained that the RFA had not been finalized, but would be publicly available.

Ms. Nichols asked for a flow of information so the veterans could point out issues that might have been missed. She asked for more information about the Deployment Health Working Group meetings, e.g. when and where they are being held, if they were involved in the IOM contracting process, etc. She also inquired about the Committee's expert panel's activities. Chairman Binns stated that the Committee needed to make better use, in a formal way, of the expert panelists. He stated the panelists had been consulted individually on certain questions, but there had not been a formal process to solicit their collective wisdom. He noted that telephone meetings with each panelist had occurred very early after the Committee's inception (2002) to brainstorm ideas and get initial reactions. He indicated that a more regular and formal interaction was a good idea. Dr. Haley commented that Dr. Golomb, former RAC Scientific Director, had worked extensively with these panelists in 2002 to help form the questions addressed by the Committee. He stated that this was a very informative time, using the expertise of very prominent and knowledgeable neuroscientists. He noted that they hadn't been involved recently, but the Committee was still implementing the roadmap that was laid out back in 2002. Mr. Graves noted that their assistance was needed to focus the Committee's future work. Dr. Steele noted that the Committee did interact with these individuals informally, for advice on specific matters.

Chairman Binns thanked everyone for attending the meeting.

The meeting adjourned at 12:55 p.m.

## Appendix A

### Presentation 1 – Lea Steele

## Exposures and Gulf War Illnesses

---

Lea Steele, Ph.D.  
September 19, 2005

\*\*\* RAC-GWVI

### Approaching the Big Picture

---

- > Context for understanding potential relationship between wartime exposures and Gulf War veterans' health
  
- > The work of the RAC-GWVI: *Where we've been and where we're going*

\*\*\* RAC-GWVI

### Work of the RAC-GWVI: Identify Research Priorities for Gulf War Illnesses

---

*Research to address questions related to:*

- > *Nature of*
- > *Causes of,*
- > *Treatments*

*for Gulf War veterans' illnesses*

\*\*\* RAC-GWVI

### Why Address the Causes of Gulf War Illnesses?

---

- > To shed light on the physiological nature of veterans' conditions
  
- > To assist in identifying treatments
  
- > To prevent similar problems in future deployments

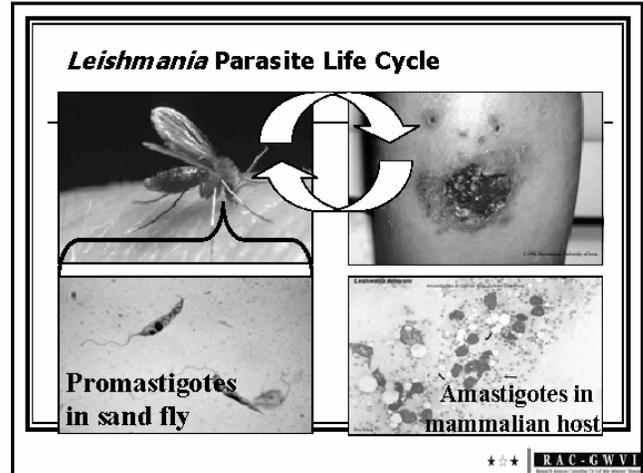
\*\*\* RAC-GWVI

**Systematic review of exposure-related topics**

*The Committee has considered evidence related to a variety of exposures in theater .....*

\*\*\* RAC-GWVI





**Committee has reviewed large amount of information on exposures potentially relevant to Gulf War veterans' health**

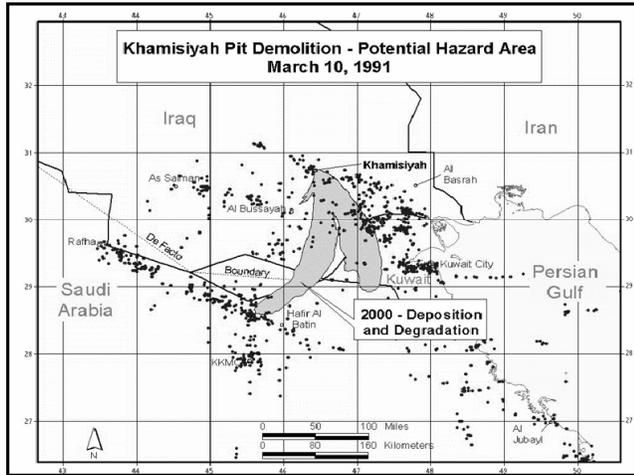
*Major types of Gulf War-related exposures considered thus far:*

- > Pyridostigmine bromide
- > Nerve agents
- > Pesticides/repellants
- > Vaccines
- > Oil well fires
- > Depleted uranium
- > Infectious agents

**Table 10. Population Studies Assessing Relationships of Multiple Exposures in Theater to Gulf War Veterans' Illnesses**

Population Studied	Sample Size	Health Measure	Association with Self-Reported Exposures		
			Chemical Weapons	PB	Pesticide Use
*Air Guard veterans <sup>203</sup>	1,002	severe CMI	+	+	+
		mild/moderate CMI	+	+	+
*Army veterans from New England, New Orleans <sup>244</sup>	291	neurological and musculoskeletal symptoms	+	--	+
Australian veterans <sup>24</sup>	1,456	functional impairment	+	+	+
Iowa veterans <sup>130</sup>	1,896	cognitive dysfunction	+	+	+
*Navy Seabees <sup>60</sup>	11,888	CMI (modified)	+	+	+
*Navy construction battalion <sup>107</sup>	249	1 or more of 3 defined syndromes	+	+	+
*New England Army veterans <sup>361</sup>	1,290	CMI (modified)	na	+	na
*Pacific Northwest veterans <sup>201</sup>	354	unexplained illness	--	+	+
UK male veterans <sup>340</sup>	2,735	CMI (modified)	+	+	+
*UK veterans <sup>22</sup>	7,971	symptom severity	na	+	+

CMI: chronic multisymptom illness as defined by Fukuda et al.<sup>24</sup>  
 +: statistically significant association; --: association not statistically significant; na: association not assessed  
 \* Indicates analyses controlled for possible confounding due to concurrent exposures



April 2003 Report from DOD Special Assistant for Gulf War Illnesses

## Environmental Exposure Report

### Pesticides

Environmental Exposure Reports are reports of what we know today about certain events of the 1990-1991 Gulf War. This particular environmental exposure report focuses on the use of pesticides by US military personnel and the resulting exposures to these compounds. Our goal is, to the extent possible, to determine if the pesticides used during the Gulf War contributed to unexplained illnesses reported by some Gulf War veterans. This is an interim, not a final, report. We hope that you will read this and contact us with any information that would help us better understand the events reported here. With your help, we will be able to report more accurately on the events surrounding pesticide use and exposures. Please contact my office to report my new information by calling:

**1-800-497-6261**

Dale A. Vreiser  
Acting Special Assistant for Gulf War Illnesses, Medical Readiness, and Military Deployment  
Department of Defense  
200 1023 1000014  
Ver 1.1

★ ★ ★ RAC - GWVI

Table 7. Studies of Chronic Effects of Low-Dose Sarin Exposure in Animals

Study	Year	Animal Model	Major Finding
Bunthoff <sup>20</sup>	1978	monkey	Persistent effects on electroencephalograph readings
Husain <sup>21</sup>	1983	mouse	Delayed development of spinal cord lesions
Jones <sup>22</sup>	2000	rat	Chronic reduction in nicotinic ACh receptor binding in cerebral cortex
Kassa <sup>23</sup>	2000	rat	Chronic alteration in immune function (lymphocyte proliferation, bactericidal activity of macrophages)
Kassa <sup>24</sup>	2000	rat	Persistent changes in DNA and protein metabolism in liver tissues
Kassa <sup>25</sup>	2001	rat	Subtle chronic signs of neurotoxicity and immunotoxicity with repeated exposures
Kassa <sup>26</sup>	2001	rat	Impaired spatial memory
Coen <sup>27</sup>	2002	rat	No persistent effects on reported indices of temperature regulation and motor activity
Henderson <sup>28</sup>	2002	rat	Delayed, persistent changes in cholinergic receptors in brain areas associated with memory loss and cognitive changes
Huler <sup>29</sup>	2002	guinea pig	Persistent failure to habituate on functional test battery
Sorensen <sup>30</sup>	2002	rat	Persistent increase in cerebral blood flow in specific areas
Kaira <sup>31</sup>	2002	rat	Suppression of immune response (antibody-forming cells and T cell responses) mediated by the autonomic nervous system
Roberson <sup>32</sup>	2002	guinea pig	Chronic depression of AChE activity, persistent behavioral changes (disoriented activity, increased rearing behavior)
Husain <sup>33</sup>	2003	mouse	Persistent reductions in respiratory exchange, blood AChE activity and BChE activity, NTE activity in various tissues
Sorensen <sup>34</sup>	2003	rat	Down-regulation of muscarinic receptors in hippocampus, decreased habituation
Kassa <sup>35-38</sup>	2003-2004	mouse	Chronic alteration in immune function (increase in CD19 cells, decrease in CD4 cells, decrease in mitogen-induced lymphoproliferation, increased NK cell activity)

RAC - GWVI

**Glove Box Enclosure System**

**Aerosol Generation System**

Screw Feeder  
Cyclone  
Venturi Feeder

**96-Port Nose-Only Exposure Chamber**

Nose Ports

### Diverse sources of research information considered

\*\*\*\*

- **Published research**
  - > Epidemiologic studies of Gulf War-era veterans
  - > Clinical studies of Gulf War veterans
  - > Occupational health studies related to exposures
  - > Animal studies
  - > Tissue studies
- **Research-in-progress**
- **Government reports**
  - > Various agencies (e.g. DOD, VA, HHS, GAO)
  - > Various committees (e.g. Congressional, PAC, PSQB, NIH)
  - > Foreign governments
  - > Topics related to exposures (measured and modeled), health risk assessments
- **Nongovernmental reports**
  - > RAND
  - > IOM
  - > Other

★★★ RAC-GWVI

### Moving From Information Review to Identifying Research Needs and Priorities

- **Assemble and analyze information from different sources**
  - > *Compare findings from different studies: how are they similar? how are they different?*
  - > *Weigh strengths/weaknesses of individual studies*
  - > *Evaluate nature and strength of evidence related to health effects of each type of exposure of interest – alone and in combination with other exposures*

★★★ RAC-GWVI

### Moving From Information Review to Identifying Research Needs and Priorities

- **Committee Findings and Conclusions:**
  - > **What we know from existing research**
    - *Re: Health of Gulf War veterans*
    - *Re: Effects of exposures*
  - > **What we don't know**
  - > **Research priorities** for addressing unanswered questions and health needs of ill Gulf War veterans

★★★ RAC-GWVI

### Considerations in "weighing the evidence"

- **Complex illnesses:**
  - > Clinical presentations vary: different veterans have different symptoms, signs, diagnosed conditions
  - > Illnesses may reflect different pathophysiological processes in different veterans

★★★ RAC-GWVI

### Considerations in "weighing the evidence"

- **Complex etiology:**

- > Multiple "causative" factors? not one cause → one disease

- **Single causes in some individuals?**

- *Varies with dosage*
    - *Varies with individual susceptibility*
    - *Different single causes in different individuals?*

- **Multiple causes in some individuals?**

- *Combinations of exposures vary between individuals*
    - *Dosages in those combinations vary*
    - *Individual susceptibility to combinations likely to vary*



### Current Meeting: Exposures to be Considered

- Petroleum combustion products
- Particulates
- Solvents
- Jet fuel
- Misc other

### Exposures: Questions to Consider

What evidence is there re: the potential for "Exposure X" to have contributed to the chronic symptoms affecting Gulf War veterans?

- > *Potential role as a single exposure?*
- > *Potential role in combination with other exposures?*
- > *Potential for a subset of individuals to have been particularly affected due to their location or occupation?*
- > *Potential for some individuals to have greater susceptibility to this exposure?*



## Presentation 2 – Lea Steele

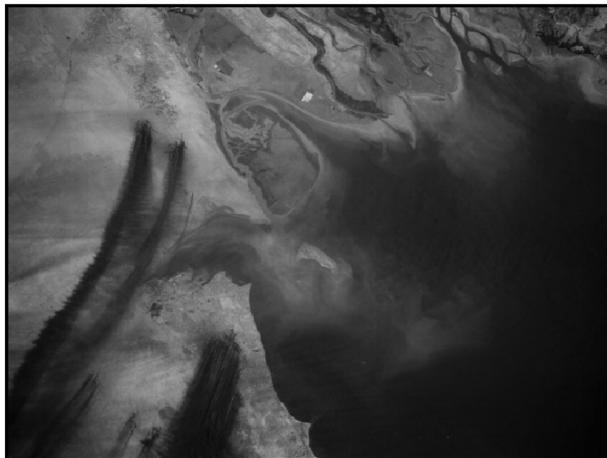
**What Do We Know About Oil Well Fires  
and the Health of Gulf War Veterans?**

**Overview and Review**

---

Lea Steele, Ph.D.

☆☆ RAC-GWVI



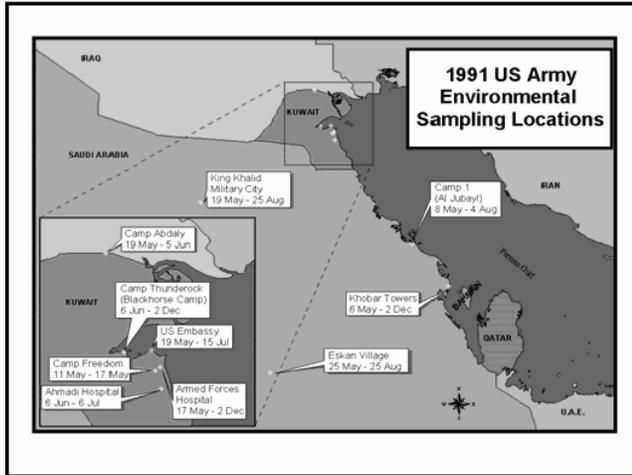
**Toxicants Found in Oil Fire Smoke**

---

- Ozone (O<sub>3</sub>)
- Nitrogen Dioxide (NO<sub>2</sub>)
- Sulfur Dioxide (SO<sub>2</sub>)
- Carbon Monoxide (CO)
- Hydrogen Sulfide (H<sub>2</sub>S)
- VOCs: Volatile organic compounds (*benzene, toluene, etc*)
- PAHs: Polycyclic aromatic hydrocarbons (*anthracene, pyrene, etc*)
- Metals (*cadmium, chromium, lead, nickel, mercury, vanadium*)
- Acidic gases/aerosols (*hydrochloric acid, nitric acid, sulfuric acid*)
- Particulate matter (*PM<sub>10</sub>, PM<sub>2.5</sub>, ultrafine particles*)

☆☆ RAC-GWVI





Exposure to Oil Well Fire Smoke: **Symptom Complexes**

Study	Exposure	Outcome	Findings
Iowa Study, 1997 (1,886 Iowa vets)	sr smoke, combustion products	cogn dysf symps FMS symps depression symps	sign prev diff (p<0.001) sign prev diff (p<0.001) sign prev diff (p<0.001)
Haley, 1997 (249 Navy vets)	sr oil smoke scaled smoke exposure	any of 3 syndromes Syndrome 2	ns p = 0.02
Nisenbaum, 2000 (1,163 Air Guard vets)	sr	mild-mod CMI severe CMI	OR = 1.29 (0.92-1.81) OR = 1.62 (0.79-3.35)
Spencer, 2001 (1,119 OR, WA vets)	eye irritation from burning oil wells	CMI	1-5 days: OR = 2.64 (1.34-5.20) 6+ days: OR = 4.47 (2.07-9.63)

☆☆ RAC-GWVI

Exposure to Oil Well Fire Smoke: **Symptom Complexes**

Study	Exposure	Outcome	Findings
Urwin, 1999 (3,284 UK vets)	sr	CMI	OR = 1.8 (1.5-2.1)
Wolfe, 2002 (945 Army vets)	sr oil fire smoke odor	CMI	OR = 2.1 (1.4-3.2)
Gray, 2002 (11,868 Seabees)	modeled self-report	BWV	bivariate: OR = 1.54 (1.31-1.80) multivar: OR = 0.44 (0.26-0.73) bivariate: OR = 2.22 (1.85-2.66) (sr) multivar: OR = 1.23 (0.91-1.65) (sr)
Kang, 2002	consumed food contaminated with oil, smoke	Neuro symp factor	73% cases vs. 21% controls

☆☆ RAC-GWVI

Exposure to Oil Well Fire Smoke: **Diagnosed Conditions**

Study	Exposure	Outcome	Findings
Gray, 2002 (11,868 Seabees)	CHPPH model	self-reported medical diagnoses	Asthma OR = 1.82 (1.23-2.69) Bronchitis OR = 1.49 (1.18-1.87)
Cowan, 2002 (873 cases, 2664 controls from CCEP)	sr and CHPPH models	clinically diagnosed	Asthma OR = 1.4 (1.1 - 1.8)
Lange, 2002 (1,560 Iowa veterans)	sr CHPPH model	symptoms of asthma, bronchitis	Asthma ORs = 1.77-2.83 (sr) Bronchitis ORs = 2.14-4.78 (sr) Asthma, Bronchitis: ORs=0.77-1.26
Kelsall, 2004 (1,456 Australian vets)	sr exposure to "SHOIL"	self-reported medical diagnoses	Asthma OR = 1.82 (1.23-2.69) Bronchitis OR = 1.49 (1.18-1.87)

☆☆ RAC-GWVI

### Summary of Epidemiologic Findings: General Points

---

- Results differ by how exposure is assessed
  - > Self reported: yes/no vs. graded exposures
  - > Self-reported exposure vs. modeled exposure
  - > Unadjusted vs. adjusted estimates (possible confounding)
  
- Results differ by health outcome of interest
  - > Respiratory symptoms, other defined symptoms types
  - > Multisymptom illness complexes
  - > Diagnosed medical conditions

★★★ RAC-GWVI

### Summary of Epidemiologic Findings

---

- 65-80% of Gulf vets report some exposure to oil fire smoke during deployment; duration and intensity vary
  
- 30% report eating food contaminated with oil or smoke

★★★ RAC-GWVI

### Summary of Epidemiologic Findings

---

- Among veterans who served in the Gulf War, exposure to oil fire smoke associated with:
  - > Short-term respiratory symptoms
  - > Diagnosed and self-reported asthma (ORs~1.4 - 2.8)
  - > Chronic multisymptom conditions (ORs~1.5 - 4.5) (possible dose-response effect—proximity and duration)

★★★ RAC-GWVI

### Oil Well Fires and the Health of Gulf War Veterans: Remaining Questions

---

- Is Gulf War-related multisymptom illness linked to exposure to smoke from oil well fires?
  - > *As single exposure?*
  - > *As a result of interaction with other exposures?*
  
- Are increased rates of asthma or other diagnosed conditions associated with exposure to oil well fire smoke?
  
- Are there additional health concerns for military personnel located very close to burning wells for an extended period?

★★★ RAC-GWVI



**Presentation 3 – Gary Friedman**



**Kuwait Oil Well Fires**

- August 2, 1990 - Iraq invades Kuwait
- January 22, 1991 - Wahfra field ignited
- February 15-17 1991 – Iraqi army ignites major oil fields
- February 24, 1991 – ground offensive begins and fires reach peak
- February 28, 1991 Kuwait City liberated

**Firefighting**

- Assessment for equipment, materials, manpower and water sources began in late February 1991.
- Fire fighting efforts commenced March 11, 1991.
- November 6, 1991 last well capped

**Oil Wells**

- Number 749
- Some burned up to 80,000 barrels of crude per day
- Flares up to 700 feet in height
- Plumes reached 12,000 feet

### **Burning Crude**

- Particulate matter
- Gases – H<sub>2</sub>S, SO<sub>2</sub>, NO<sub>x</sub>, CO, Methane
- Volatile Organics (benzene, toluene, etc)
- Poly Aromatic Hydrocarbons (PAHs)

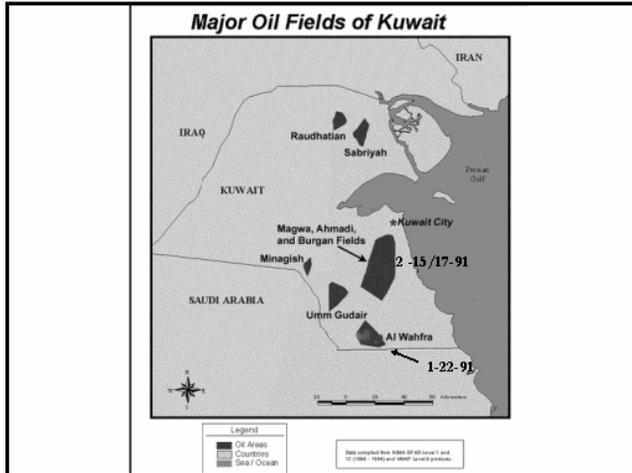
### **Texas Based Oil Well Fire Fighters – Kuwait**

- Adair Company – 39
- Wild Well Control – 38
- Boots and Coots 30

### **Adair Company**

- Most of their activity involved the Burgan, the Magwa and the Ahmadi oil fields located south of Kuwait City.

--	--	--



### Tours of Duty

- Late February 1991 through 11-8-91
- Work day 10 – 12 hours
- Tour 28 – 40 days alternated with 28 day leave

### Tours of Duty

- Adair – 39 men - avg. 98 days
- Wild Well – 38 men avg. 98 days
- Boots and Coats – 30 men avg 112 days
- Average – 105 days

### Texas Based Oil Well Fighters

- Extinguished the majority of the wells
- The largest oil fields
- High pressure wells with the largest flow of gas and oil and the largest plumes
- Longest exposure times

**U.S. INTERAGENCY AIR ASSESSMENT  
TEAM IN KUWAIT AND SAUDI ARABIA  
METHOD**

**Thirteen locations in Kuwait and Saudi Arabia, U.S. Embassies in Kuwait and Riyadh, 5 oil well fields and at various locations near oil well fields in Kuwait.**

**RESULTS (3/13 – 3/27)**

- The highest levels of VOCs were in the oil fields near oil lakes
- The only significantly elevated finding was particulates

**U.S. INTERAGENCY AIR ASSESSMENT  
TEAM IN KUWAIT AND SAUDI ARABIA  
RESULTS (3/13 – 3/27)**

**“The highest readings were recorded from measurements taken in the smoke plumes in the oil fields.”**

**Volatile Organic Compounds  
Blood Levels**

Dr. R. A. Etzel at CDC studied blood levels of VOCs of forty firefighters two hours after exposure to burning wells and compared them to Army personnel in Kuwait City 20 km from the burning wells. She compared the VOC's to 114 from a reference group in the United States.

R. A. Etzel and D. L. Ashley, "Volatile organic compounds in the blood of persons in Kuwait during the oil fire", Int. Arch Occup. Environ. Health (1994), pg 47/1-47/5.

### **Volatile Organic Compounds Blood Levels**

**Group I (Kuwait City) – 14 males 20 km from fires. Blood VOC's were lower than or comparable to median concentrations in a reference group in the United States. Only 1 smoker.**

R. A. Etzel and D. L. Ashley, "Volatile organic compounds in the blood of persons in Kuwait during the oil fires", Int Arch Occup. Environ. Health (1994), pg 47/1-47/5.

### **Volatile Organic Compounds Blood Levels**

**Group II (firefighters) – 38 males and 2 females, median distance from burning wells 10 feet during previous 24 hours, 2 hours elapsed since last exposure. During preceding 24 hours they were within 500 meters for a median of 10 hours. 37% were smokers. VOC's 3 to 4 times reference population.**

R. A. Etzel and D. L. Ashley, "Volatile organic compounds in the blood of persons in Kuwait during the oil fires", Int Arch Occup. Environ. Health (1994), pg 47/1-47/5.

### **Living Conditions**



### **LIVING CONDITIONS**

**Lived within 2 miles of the burning fields in an abandoned complex between Burqan and Ahmadi Oil fields**

**Initially no running water (trucked in)**

**Smoke filled building**

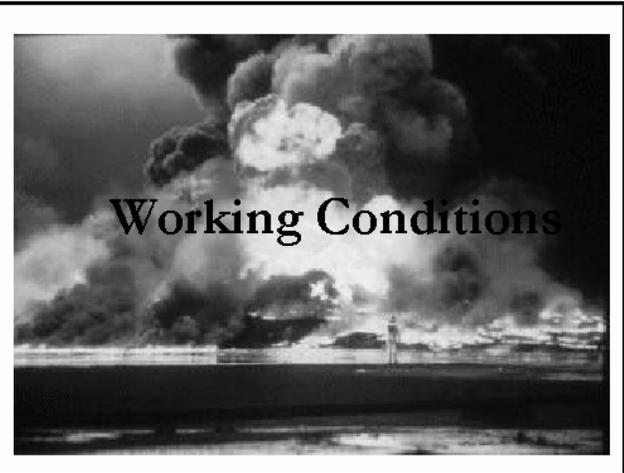
## LIVING CONDITIONS

**Drinking water – bottled**

**Food – imported – brought their own cook**

**Medical – medic on-site with first aid trailer/ambulance**

**Later in campaign – compound established at Ahmadi with 500 -600 inhabitants.**



## FIREFIGHTER PROTECTIVE GEAR

**Nomex underwear**

**Gloves**

**Hard hat**

**Leather boots**

**Work coveralls**

**No respirators**



### Heat



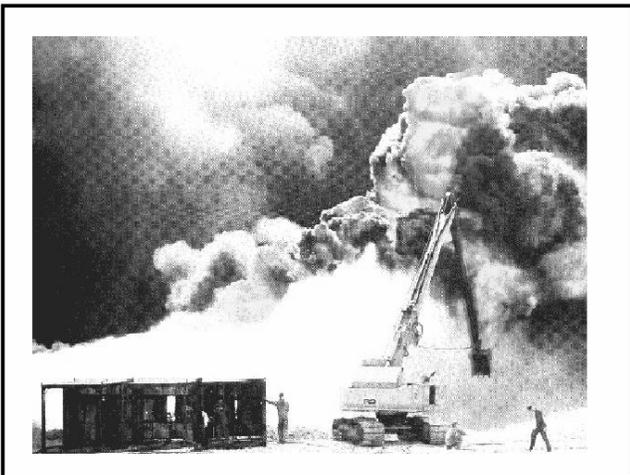
### Smoke



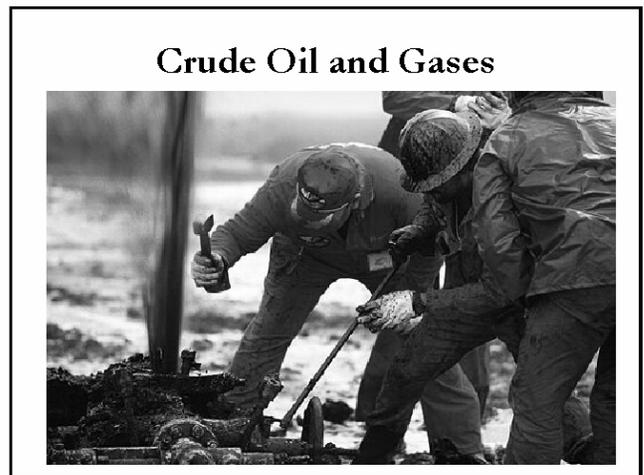
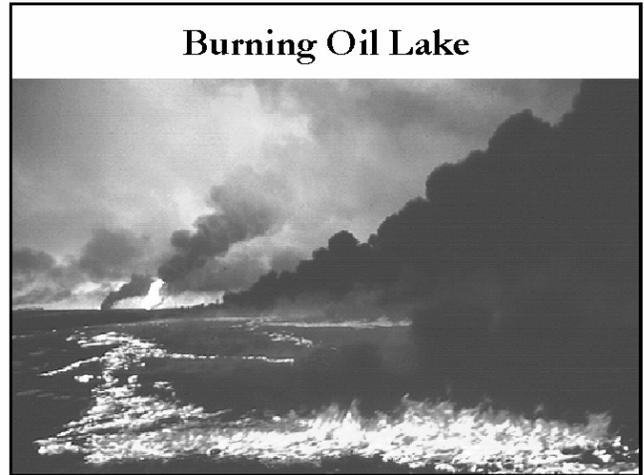
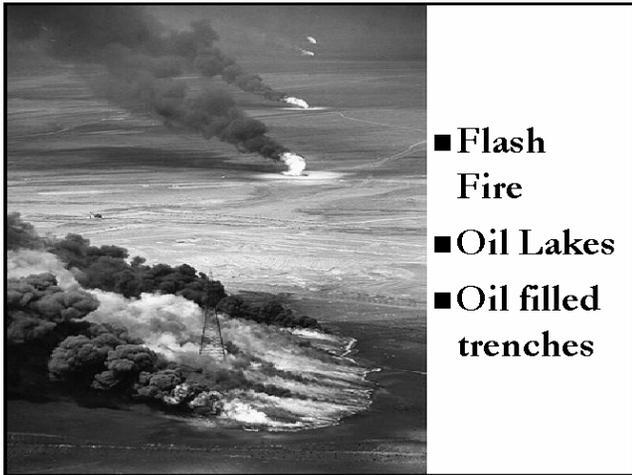
### Heat and Smoke



### Fumes and Gases



Gases and oil lake  
Risk of explosion  
And Fire



## Mines



## Canary In A Cage



## MEDICAL SURVEILLANCE

- Complete history and physical – physician Board Certified in Occupational Medicine and Internal Medicine
- CBC
- SMA-20 (glucose, BUN, Creatinine, Liver enzymes, etc.)
- Urinalysis

**MEDICAL SURVEILLANCE**

- **Pulmonary function testing (spirometry)**
- **Chest x-ray**
- **EKG**
- **Stool for O&P (as available or indicated)**

**MEDICAL SURVEILLANCE**

- Firefighters were re-evaluated during leaves between their tours of duty
- A follow up in 1994 with each of the 3 Houston based companies revealed no claims for medical problems arising from service in Kuwait.

**RESULTS From All 3 Companies**

- No objective evidence of disease**
- No reports of lost time due to illness**
- No reports of symptoms resembling "Desert Storm Syndrome"**
- No subsequent reports of any illness of delayed onset**
- No claims filed seeking compensation for any type of illness**

**Current Status**

**After Kuwait the Adair Company was sold and many of the former employees are currently employed by oil well firefighters Boots and Coots in Houston.**

### **Current Status 9-14-05**

Telephone conference with both Boots and Coots and Wild Well Control reveals no reports of Gulf War Syndrome-type illness or other chronic illness or injury arising from the Kuwait experience. Firefighters have been sent to Iraq during the current conflict without incidence.

### **Iraq**



### **Toxic Exposures**

- Burning wells
- Refinery explosions
- Pipeline fires
- Organophosphate exposure
- Cyanide
- Phosgene
- Smoke inhalation
- Irritant gases acids and alkalis

**Domestic Experience  
Toxic Fume Center  
Texas Lung Institute**

### Toxic Fume Center

- Pro active – Standing committee
- Data base of hazardous materials refineries, chemical plants, and transportation
- Stockpiled appropriate antidotes
- Coordinated with plant safety personnel
- Houston Fire Dept and Hazmat and law enforcement

### Toxic Fume Center

- Life Flight helicopters and ambulances
- Decontamination facilities
- Level 1 trauma emergency center
- Burn unit
- Tertiary care hospital
- Multi specialty medical support







### Catalytic Cracking Unit



### Flare Stack



### Flare Stacks



**Refinery Fire**



**Refinery Fire**



**Petrochemical Plant**



During the past 25 years evaluation of thousands of Texas refinery and chemical plant workers exposed to crude oil, and its products of combustion have failed to reveal a pattern similar to "Gulf War Syndrome" in a civilian population.

### SUMMARY

The majority of wells were controlled by a contingent of experienced oil well firefighters from Houston, Texas. They were in Kuwait significantly longer than other fire fighting teams. They extinguished high pressure and high volume wells.

### SUMMARY

No significant illnesses have been reported from this cohort. Specifically no complaints resembling "Gulf War Syndrome"

### Military





## Literature

D.M. Spektor, A Review of the Scientific Literature As It Pertains to Gulf War Illnesses, vol. 6, Oil Well Fires  
National Defense Research Institute  
(RAND)

### RAND – VOC's, PAH, Pollutants

The concentrations of VOCs, polycyclic aromatic compounds, metals, and criteria pollutants were much lower than initially presumed, considering the magnitude of the fires.

D.M. Spektor, A Review of the Scientific Literature As It Pertains to Gulf War Illnesses, vol. 6, Oil Well Fires (Nat. Def. Research Inst. – RAND)

### RAND – Levels Same or Lower Than U.S.

The maximum concentrations measured in the Persian Gulf region are virtually the same levels found in suburban locations in the United States, lower than those found in large urban centers in the United States, and much lower than the U.S.-recommended occupational levels.

D.M. Spektor, A Review of the Scientific Literature As It Pertains to Gulf War Illnesses, vol. 6, Oil Well Fires (Nat. Def. Research Inst. – RAND)

### **RAND Lower Than Occupational**

The data show that the concentration of the pollutants present in the environment as a consequence of the oil well fires fell below the exposure limits for hazardous substances in the workplace recommended by the National Institute of Occupational Safety and Health, Occupational Safety and Health Administration, or American Conference of Governmental Industrial Hygienists.

D.M. Spektor, A Review of the Scientific Literature As It Pertains to Gulf War Illnesses, vol. 6, Oil Well Fires (Nat. Def. Research Inst. - RAND)

### **RAND - Particulates**

- “Measurements at all monitoring sites show that particulate concentrations were much higher than ambient levels in the U.S. The high density of atmospheric particles did not result from the oil fires; rather, it is characteristic of the region itself. Comparison of measurements taken in 1991 and in 1994, when the fires had long been extinguished, show similar average values.”

■ D.M. Spektor, A Review of the Scientific Literature As It Pertains to Gulf War Illnesses, vol. 6, Oil Well Fires (Nat. Def. Research Inst. - RAND)

### **Environmental Exposure Report Oil Well Fires Bernard Rostker Special Assistant for Gulf War Illness (DOD)**

### **US Army Environmental Hygiene Agency (USAEH)**

- Maximum concentration of air contaminants (other than particulates) were similar to levels found in suburban location and below those found in large urban areas.
- Over 4000 samples
- Concentration of pollutants in area of US troops and civilians fell below ACGIH, OSHA or NIOSH workplace exposure limits

Environmental Exposure Report Oil Well Fires Bernard Rostker (DOD)

### Particulate Matter

- Kuwait has one of the highest background levels of particulates in the world due to sand.
- Only 22% of PM<sub>10</sub> was due to soot.

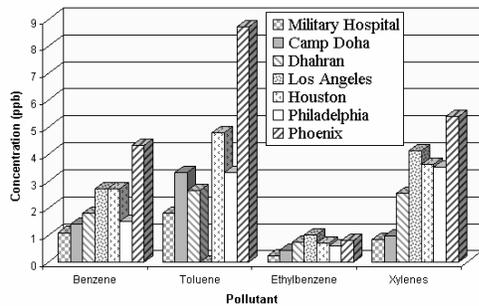
Environmental Exposure Report Oil Well Fires Bernard Rostker (DOD)

### Polyaromatic Hydrocarbons (PAH)

- Porier et. al. reported blood levels of PAHs on 61 army soldiers in Persian Gulf in 1991. Compared to soil and air measurements from areas where deployed. No evidence of increases in blood PAHs.

Environmental Exposure Report Oil Well Fires Bernard Rostker (DOD)

### Volatile Organic Compounds (VOC)



### Risk Assessments

- Risk levels were calculated for all US troop units and compared against levels determined to be safe by the US EPA.
- “In all cases troop unit excess cancer and non-cancer risk levels were below their respective US EPA safe risk levels”

Environmental Exposure Report Oil Well Fires Bernard Rostker (DOD)

**B. Rostker Special Assistant for  
Gulf War Illness Dept. of Defense**

“The exposures that troop units received from oil fires and other industrial sources in the Gulf should not, by themselves, have caused health problems.”

Environmental Exposure Report Oil Well Fires Bernard Rostker (DOD)

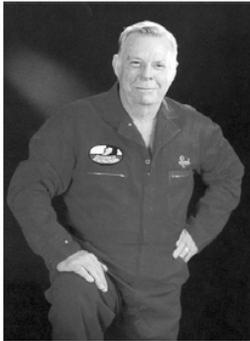


**Canary In A Cage**



**Raw or burning crude oil  
should be dismissed as a  
cause for Gulf War  
Syndrome**

**Mr. Red Adair**  
**1915 - 2004**



Presentation 4 – Lea Steele

**Fuel Combustion Products, Particulates**

Exposures and Epidemiologic Findings  
in Gulf War Veterans

---

**Lea Steele, Ph.D.**

September 19, 2005

☆☆ RAC-GWVI

**Exposure to Hydrocarbon Fuel Combustion Products**

---

Sources of Exposure:

- Oil well fires (partially combusted crude oil)
- Tent heaters, cooking stoves (combusted gasoline, kerosene, diesel, jet fuel)
- Exhaust emissions from military vehicles and aircraft
- Emissions from generators
- Open burning of trash, wastes

☆☆ RAC-GWVI

**Hydrocarbon Fuel Combustion: Primary Compounds of Concern**

---

Complex mixtures of gaseous compounds and particulates

- O<sub>3</sub>, CO, CO<sub>2</sub>, SO<sub>2</sub>, NO, NO<sub>2</sub>, H<sub>2</sub>S
- VOCs, PAHs
- Particles of varying chemical composition and size

☆☆ RAC-GWVI

**Hydrocarbon Fuel Combustion**

---

IOM Report on Fuel, Combustion Products, and Propellants (2005):

*Sufficient evidence to conclude that there is an association between combustion products and lung cancer*

*Limited/suggestive evidence of an association between combustion products and cancers of nasal and oral cavities, bladder cancer, and low birthweight/pre-term births*

☆☆ RAC-GWVI

### Tent Heater Emissions

---

- Exposures varied seasonally; in cold weather, tent heater exposures could have been continuous for 8 or more hours, over days – months
- Mumford et al (J Toxicol Env Health 1992;36:151) reported that organic emissions from unvented kerosene heaters are mutagenic

### Emissions from unvented tent heaters

---

- 2 studies from Lovelace Respiratory Research Institute
  - Zhou Y, Cheng YS. Aerosol Science and Technology 33:510-524 (2000)
  - Cheng YS, Zhou Y, et al. Aerosol Science and Technology 35: 949-957 (2001)
- Experiments simulated and characterized emissions from heaters used inside of Army tent
- Tested 3 types of heaters, 3 types of fuels (kerosene, JA-1, JP-8)

### Emissions from unvented tent heaters

---

- Results:
  - > Emissions varied with type of fuel, type of heater, and temperature
  - > Convection heaters emitted more NO and SO<sub>2</sub> than radiant heaters, less CO and particulates
  - > NO<sub>x</sub>, CO, and SO<sub>2</sub> exceeded air quality standards when tent doors were closed; but did not exceed 24-hour exposure standards
  - > Most particulates were in the fine range (peak ~0.2 - 0.3 microns), with some in the ~10 micron range. Levels exceeded 24-hour standards when door closed, close to standards when door open

### Emissions from unvented tent heaters

---

- Chemical Analyses of Particulates:
  - > Large amounts of sulfur (most as sulfates); mostly confined to smaller particles
  - > High amount of ammonium
  - > Elemental and organic carbons
  - > Also silica, aluminum, iron, lead

**Emissions from Tent Heaters: Epidemiologic Studies**  
**How many Were Exposed?**

Study	Population	Exposure	
Gray, 1999	527 Seabees	Airplane fuel burned in tent heaters	20.7%
Kroenke, 1998	18,495 CCEP registrants	Fumes from tent heaters	73.0%
Proctor, 1998	186 Devers, 66 New Orleans Gulf War Vets	Smoke from tent heaters	Devers 69.8% New Orleans 50.0%
Unwin, 1999	3,294 U.K. Gulf War Vets	Exhaust from heaters or generators	78.2%
Vasterling, 2003	72 LA reservists	Smoke from tent heaters	56.9%
Wolfe, 2002	945 Army Gulf War Vets	Heater in tent	61.6%

**Emissions from Tent Heaters:**  
**Association with Health Outcomes**

Study	Outcome	Exposure	Findings
Proctor, 1998 (220 Army vets)	symptoms (groups)	smoke from tent heaters	Sign. correlated with cardiac, neurological, and pulmonary symptoms ( $p < 0.001$ )
Unwin, 1999 (3,294 UK vets)	CMI	exhaust from heaters	OR = 1.9 (1.6-2.2)
Spencer, 2001 (1,119 ORVA vets)	CMI	diesel heater kerosene heater pothelly heater cleaned heaters	OR = 1.78 (0.93-3.42) OR = 1.92 (0.93-4.00) OR = 2.31 (1.14-4.66) OR = 2.41 (1.29-4.52)
Gray, 2002 (11,868 Seabees)	GWV	jet fuel burned in tent heaters	OR = 2.12 (1.81-2.49) (unadj) OR = 1.11 (0.88-1.38) (saturated)
Wolfe, 2002 (945 Army vets)	CMI	heater in tent	OR = 1.6 (1.0-2.5)

**Summary: Tent Heaters**

- > 50% of troops report exposure to fumes from tent heaters (lower in Navy personnel)
- Exposure to tent heaters in theater associated with:
  - > Cardiac, neurological, and pulmonary symptoms
  - > Chronic multisymptom illness (ORs ~ 2.0)
- Compounds of potential concern include CO, SO<sub>x</sub>, NO<sub>x</sub>
- Particulate levels inside tents exceeded NAAQS standards

**Particulate Exposures in the Gulf War**



### Particulate Exposure in the Gulf War

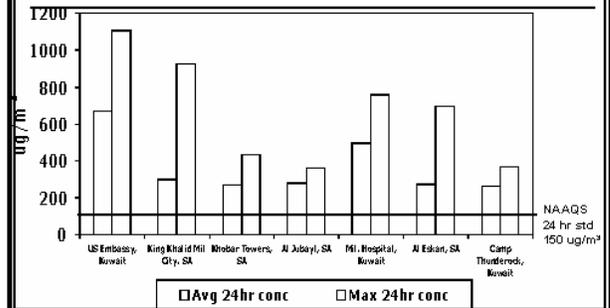
- Primary source of particulates in theater was the natural environment – blowing sand and dust (*USAEHA est: 75%*)
- Naturally occurring particulate levels in the region are among the highest in the world
- Respiratory illnesses, “Kuwaiti Crud” common among troops first entering the region

### Particulate Exposures in the Gulf War

- Other Sources:
  - > Oil well fires (*USAEHA est 23%*)
  - > Tent heater emissions
  - > Industrial pollution
  - > Engine exhaust

### Measured Total Particulates in Theater, May-Oct 1991

PM10 Concentrations by Site



Source: Particulate Matter Exposure Final Report, DoD, 2002

### Health effects of particulates

Numerous studies have linked particulate exposure to:

- ER visits for respiratory and cardiovascular conditions
- Increased death rates during acute elevation of particulates
- Aggravation of chronic respiratory conditions

### Health effects of particulates depend on:

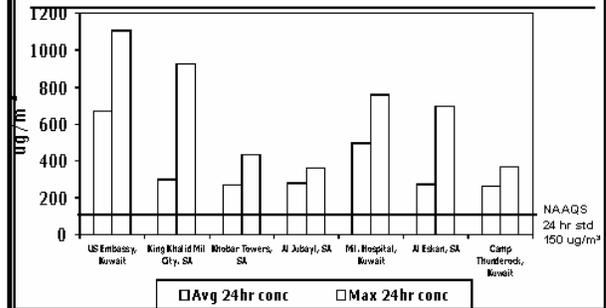
- > Concentration of exposure
- > Duration of exposure
- > Physical and chemical properties of particle
  - Particle size
  - Chemical composition
  - Surface characteristics

### Health effects in relation to particle size

- **PM<sub>10</sub>** – Particles, diameter < 10 microns, > 2.5 microns  
 Can be inhaled into and accumulate in the lungs
- **PM<sub>2.5</sub>** – Fine particles, diameter 0.1 – 2.5 microns  
 Can lodge more deeply into alveoli
- **Ultrafine particles** – Diameter < 0.1 microns  
 Can cross pulmonary epithelium and enter circulatory system  
 Recent studies indicate potential for systemic inflammatory effects, direct entry into brain

### Measured Total Particulates in Theater, May-Oct 1991

#### PM10 Concentrations by Site



Source: Particulate Matter Exposure Final Report, DoD, 2002

### Health Effects of Sand/Particulates in Gulf War Veterans?

#### Al Eskan Disease: Desert Storm Pneumonitis and Dirty Dust

- In 1992, COL (Dr.) Andreas Korenyi-Both described an illness among troops housed in Al Eskan village (SA) apartment buildings that had been uninhabited for previous decade
- Approximately 2/3 of soldiers ill with symptoms of respiratory infection within 48-72 hours of arrival
- Most recovered with antibiotic treatment; 1% relapsed 5-6 weeks after initial onset and were unresponsive to treatment
- Dr. Korenyi-Both hypothesized that soldiers' exposure to mix of fine dusts and pigeon droppings triggered immunopathologic reactions resulting in a unique illness, Al Eskan disease

### Al Eskan Disease:

#### Desert Storm Pneumonitis and Dirty Dust

- Dr. Korenyi-Both's analyses of Al Eskan sand indicated a very fine grain structure (0.1 – 0.25 microns), high CA levels. Bacteria and fungi species were isolated from the particles.
- In later publications, Dr. Korenyi-Both hypothesized that this fine sand could have acted as a carrier of chemical agents (or other exposures, including biological agents).
- The fine sand "carrier" would have enhanced the effects of the agents, increasing toxicity and delivered dosage.

**Al Eskan Disease:  
 Desert Storm Pneumonitis and Dirty Dust**

- Dr. Korenyi-Both's hypotheses have not been formally studied
- Government officials have criticized his theories for their reliance on speculation rather than data
- Recent government research on properties of sand in the region and its potential to act as a carrier of environmental contaminants

**Epidemiologic Studies:  
 Association of Health Outcomes with Sand Exposure**

Study	Exposure	Outcome	Findings
Gray, 1999 (527 Seabees)	sandstorms	fatigue forgetfulness sleepy all time rash muscle pain night sweats PTSD	OR = 2.7 OR = 2.1 OR = 2.3 OR = 2.7 OR = 2.7 OR = 2.5 OR = 4.1
Gray, 2002 (3,831 Seabees)	sandstorms	GWII	OR = 2.63 (2.09-3.3) unadj OR = 1.70 (1.26-2.25) saturated model
Kelsall, 2004 (1,456 Austr. GW vets)	dust storms	ECRHS defin. suggesting asthma	OR = 1.1 (0.8-1.7)
Suadicani, 1999 (667 Danish GW vets)	sand or dust storm	Neuropsych symptoms	Sign bivariate association with number of symptoms, $p < 0.01$

**Previous RAC Presentations Related to  
 Sand/Particulate Exposures**

- USACHPPM (2004) Measured particulates from oil well fires
- M. Sopori (2004) Lovelace Respiratory Research Institute: Inhalation of crystalline silica activates the immune system; silicosis results from second phase of response that does not require sustained immune activation
- J. Lewis (2004) University of New Mexico: Penetration of inhaled DU into the brain is enhanced when occurs with inflammation in the nasal cavities

**Summary:  
 Particulate Exposures in the Gulf War**

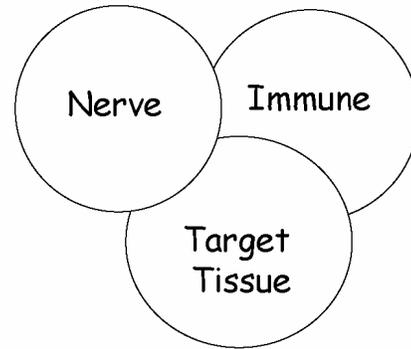
- Multiple sources of particulate exposure during the Gulf War
- Ambient particulate levels in the region among the highest in the world
- Kuwaiti sand is unique: fine "dust", highly mineralized
- Little epi information: some indication of association of chronic symptoms with s/r sandstorm exposure
- Recent research evaluates relationship of particulates to systemic and neuro inflammation

**Presentation 5 – Bellina Veronesi**

Particulate matter and neurogenic inflammation ...  
oxidative stress-mediated toxicity

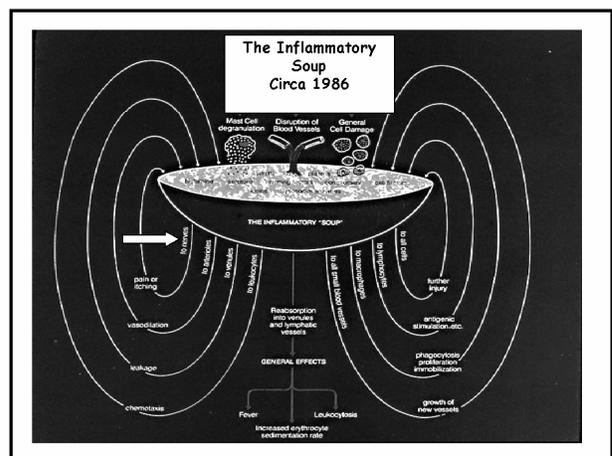
Bellina Veronesi  
U.S. Environmental Protection Agency  
Neurotoxicology Division  
Research Triangle Park, NC

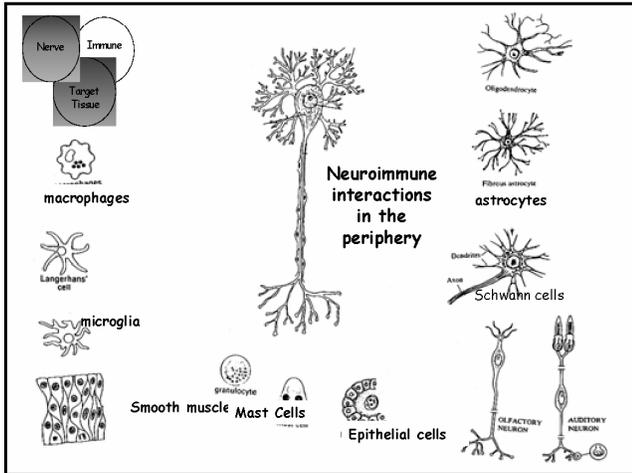
veronesi.bellina@epa.gov



"Ruber et tumor cum  
colore et dolore"

-Cornelius Cesus 35 B.C.



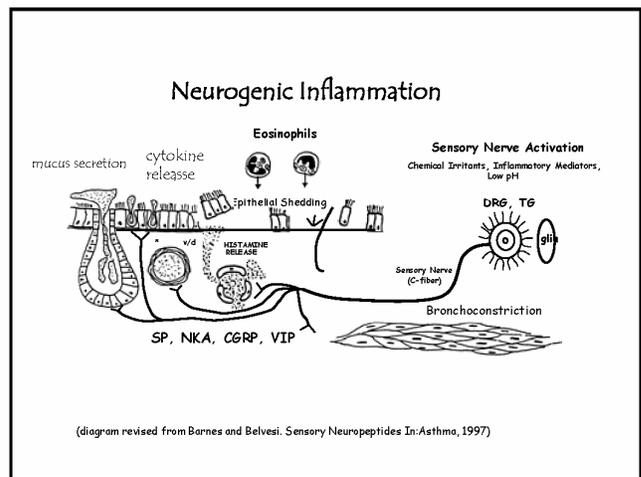


**Neurogenic Inflammation (NGI)**

- What is it?
- Where does it happen?
- Why does it happen?

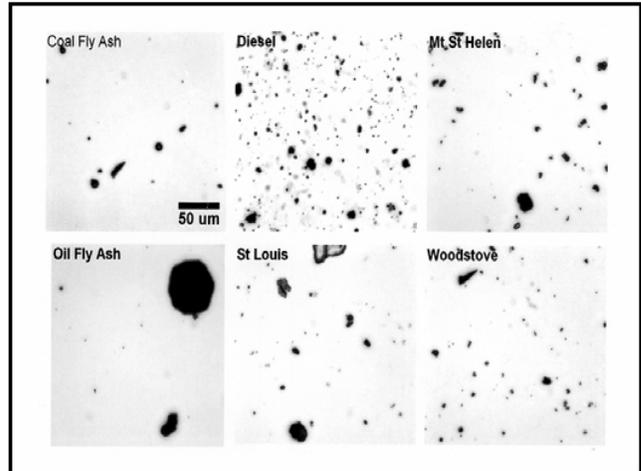
**Vanilloid (VR1 capsaicin) receptors**

**BIPOLAR NEURON (SENSORY—AFFERENT)**



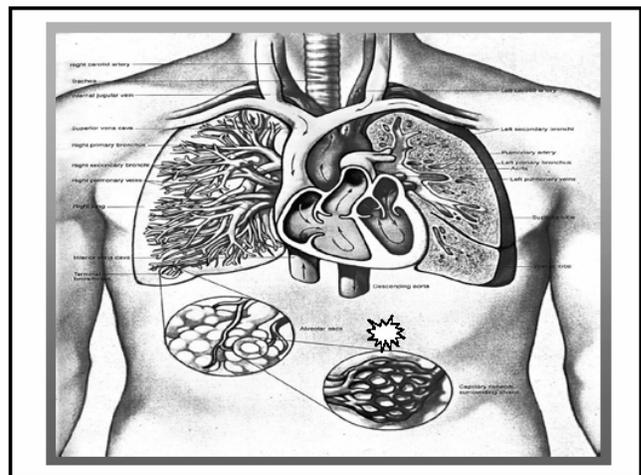
### Particulate Matter (PM)

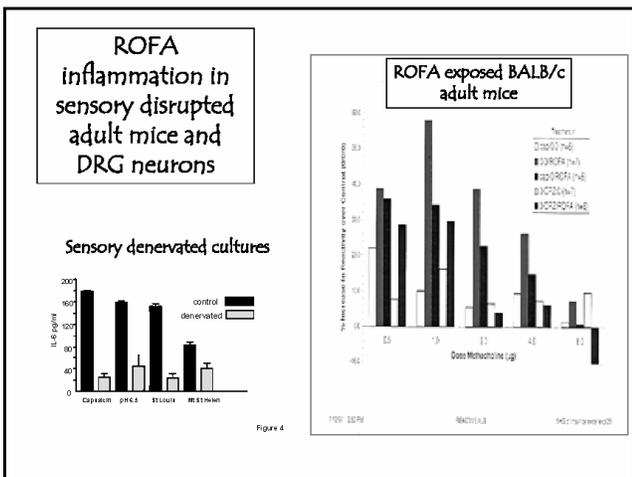
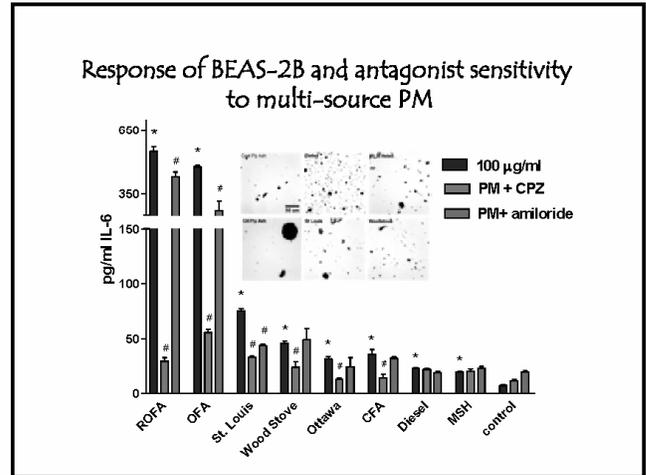
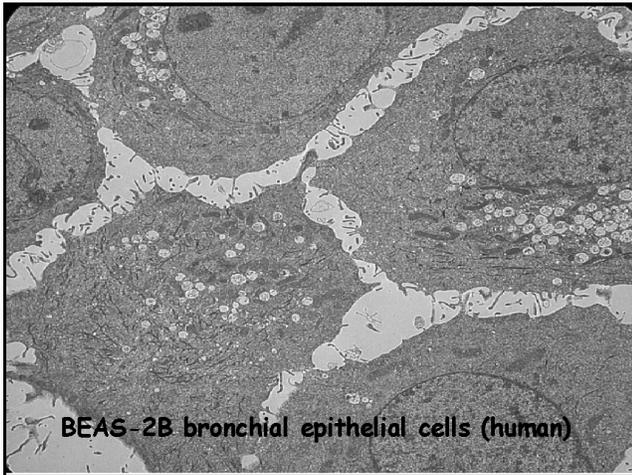
- A major concern of the US EPA
- Epidemiologically associated with increased respiratory symptoms and mortality, world-wide...cost burden
- Strong susceptible population (e.g. elderly, young, pre-existing conditions like asthmatics, cardiopulmonary, smokers)
- Multi-source PM (Industrial emission, naturally occurring, botanical, ambient) with different pollutants
- Uniform degree of mortality and morbidity

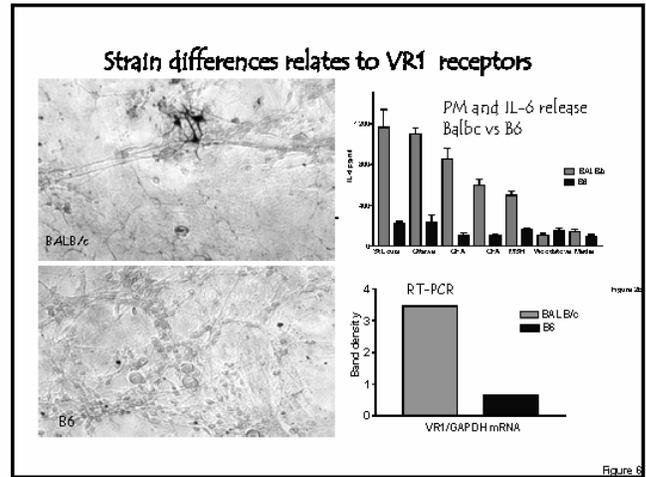
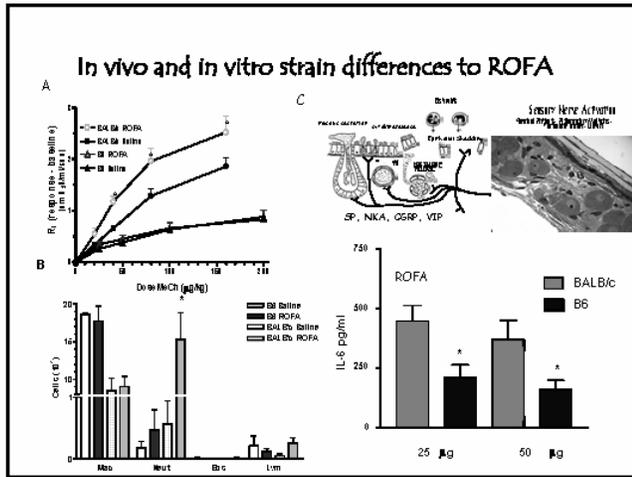


### Particle size and number important

- Surface area
- Deposition
- Proximity
  - CO<sub>2</sub>/O<sub>2</sub> interface
  - venous circulation







**PM Research Summary 1999-2003**

**PM airway inflammation**

- Non-neural cells have VR1 receptors
- PM toxicity is neurogenically mediated via VR1
- susceptible populations: genetic component, VR1 mediated

**Particulate matter and CNS neurodegeneration**

**oxidative stress ..a culpable mechanism**



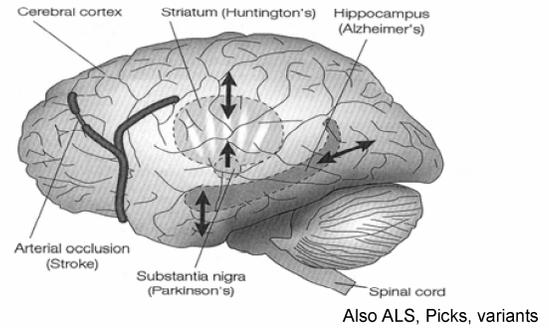
"The perfect storm"



- High energy demands (transmission, conduction)
- Low levels endogenous scavengers
  - High lipid content
  - Non-replication of neurons
- Highly reactive cells (microglia)-differentially distributed

◇

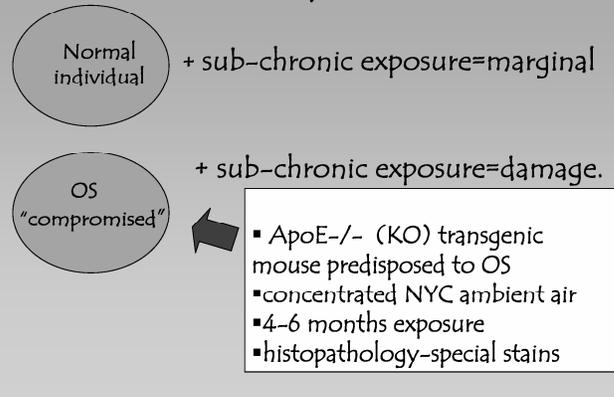
Oxidative stress and selective neurodegeneration

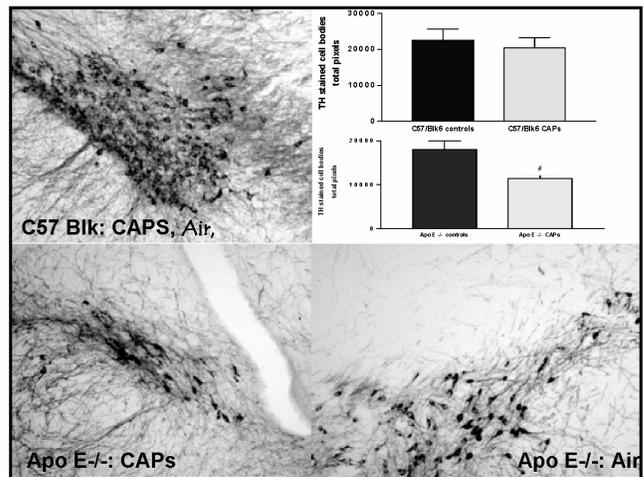
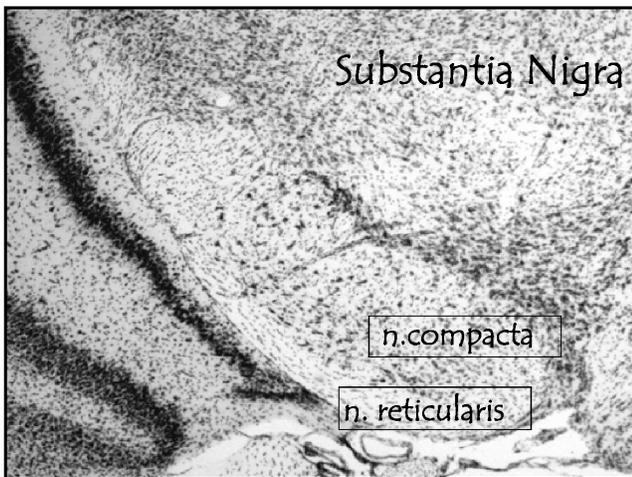
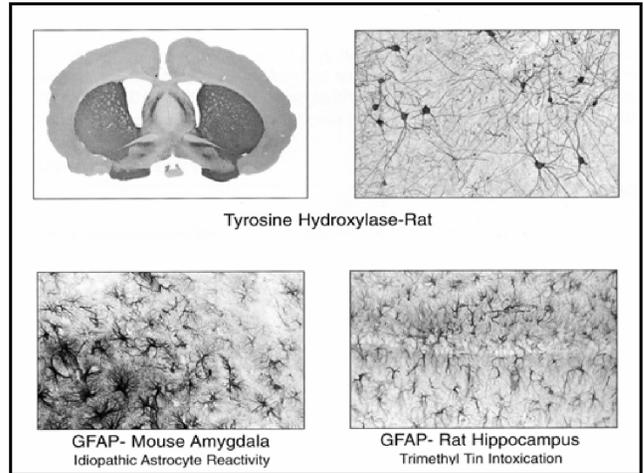
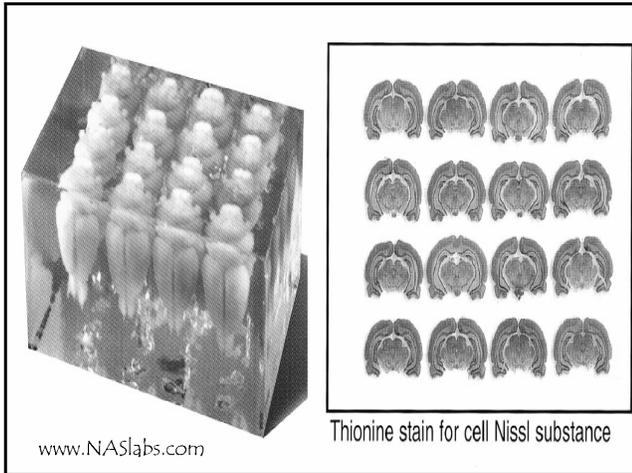


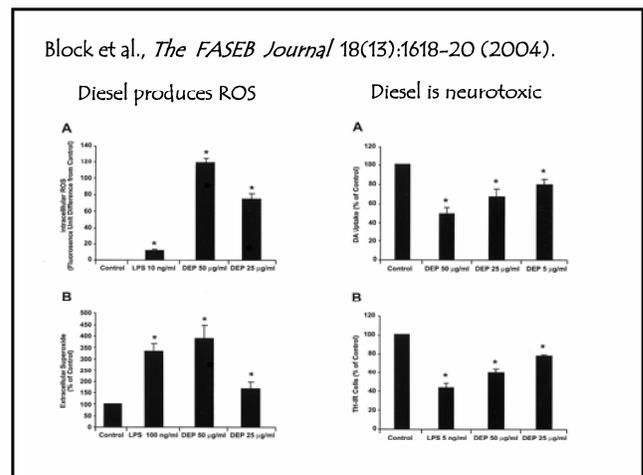
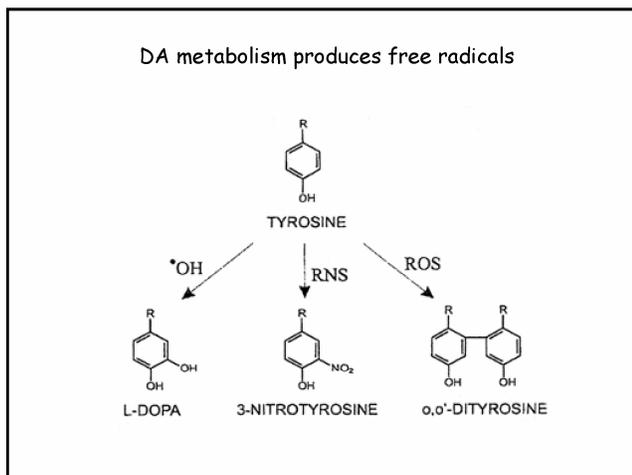
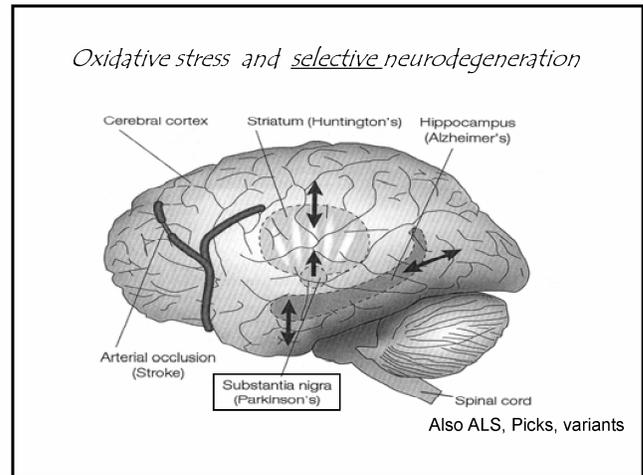
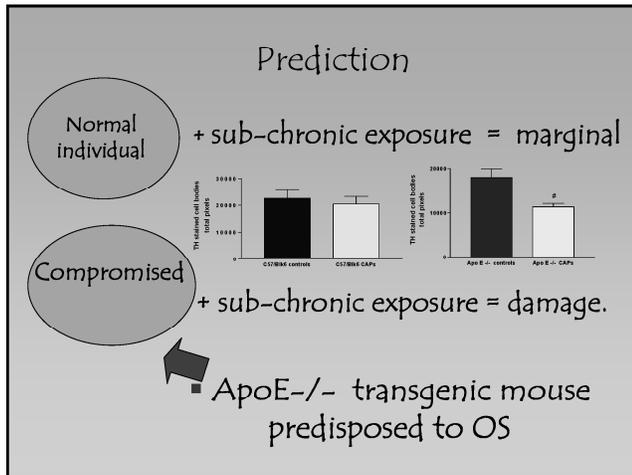
Particulate matter  
 and CNS neurodegeneration

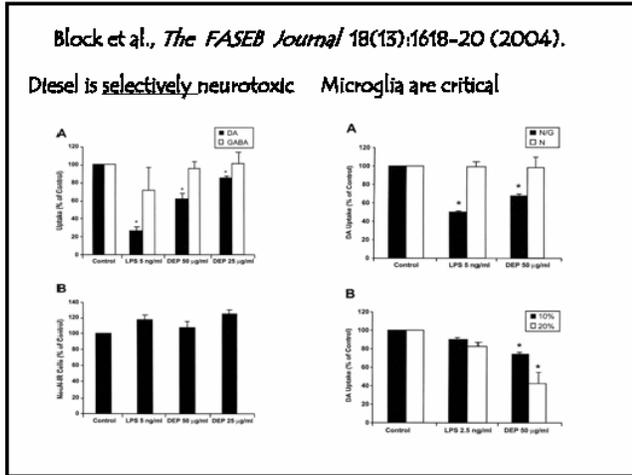


Prediction







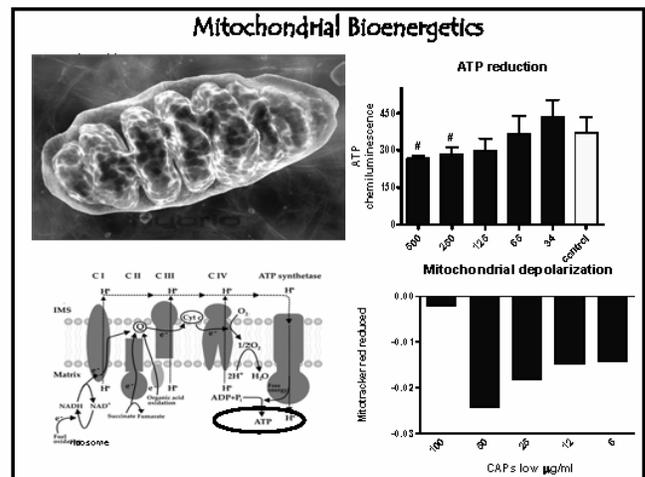


**Microglia—The CNS macrophage**

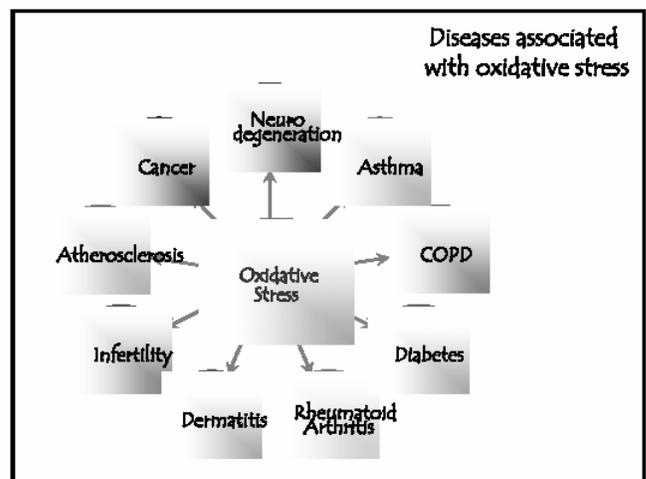
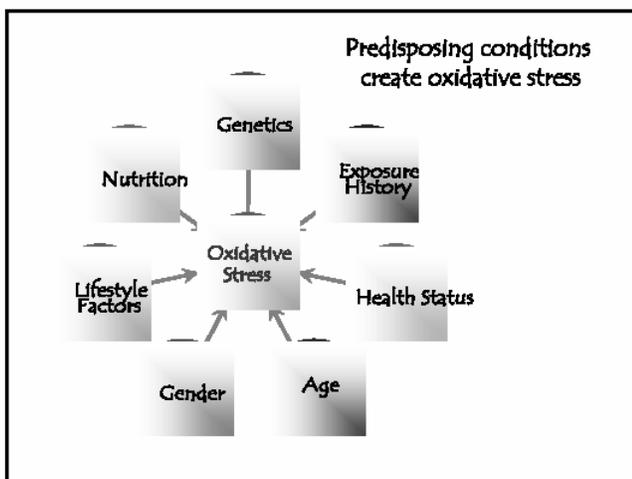
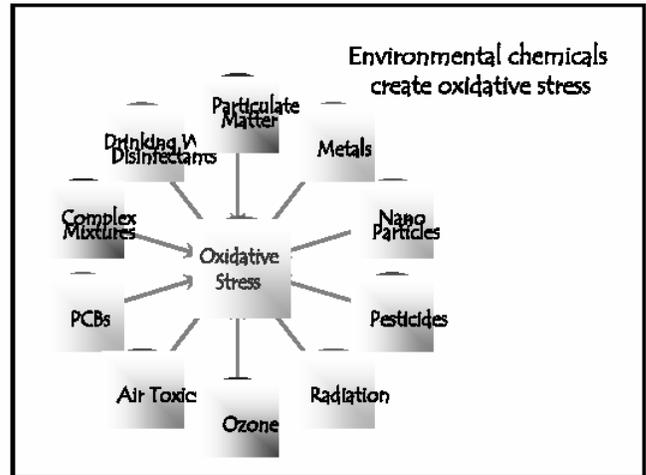
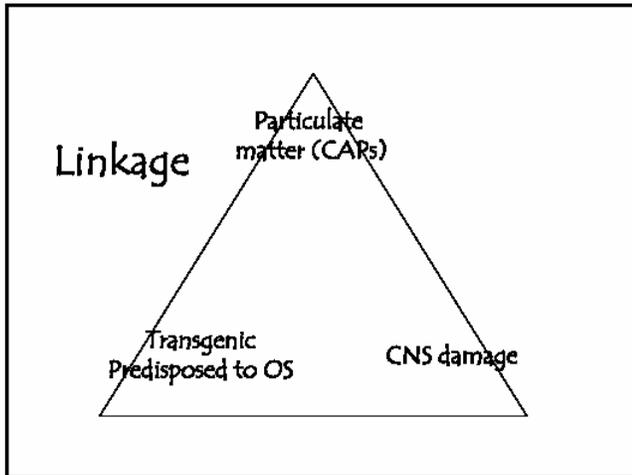
- Oxidative Burst (NADPHox mediated)
- Free radicals, super-oxides
- ROS, RNS, iNOS, NO
- over-expression of transcription factors e.g., AP-1, NFkB, Sp1, p-CREB
- Release of inflammatory cytokines, (Innate Immunity-neurotoxic)
- Glial proliferation-clusters, scarring
- ROS damage to energy-sensitive neurons (mesencephalic, SN, CA1)

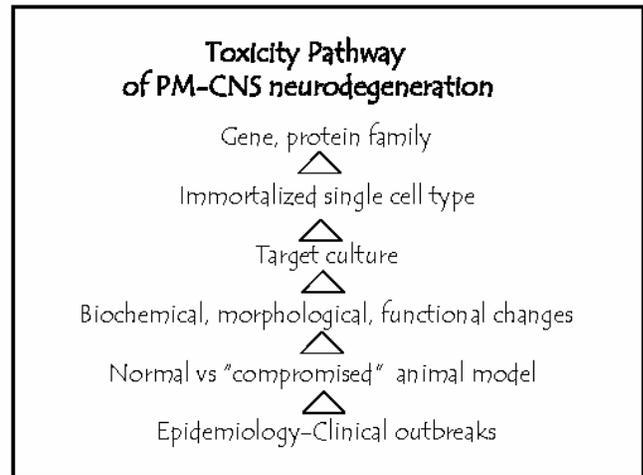
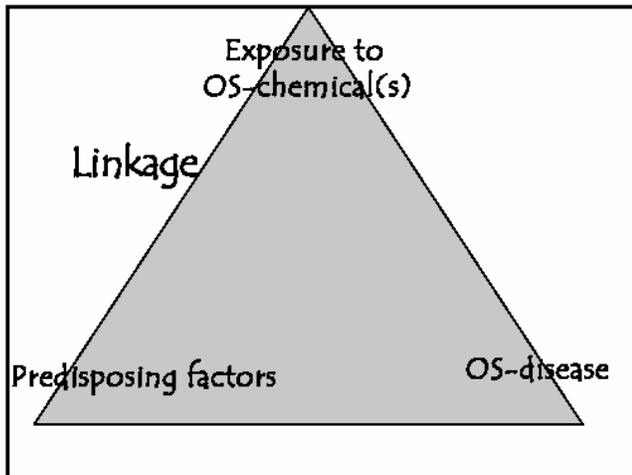
**MATERIALS AND METHODS**

- CAPs collected on site and ranked (high, low) NFkB increases Immortalized mouse CNS microglia (BV2)
- Exposed and assayed for immediate, delayed OS changes cytokine release
- Exposed and examined with TEM
- Universal (affymetrix) microarray
- Bioinformatics









**Colleagues**

NYU-Sterling Forest (LC Chen et al., )

NIEHS-Pharmacology (J. Hong et al., )

Duke University-Neurobiology, School of Medicine  
(S. Simon, M. Oortgiesen et al., )



**Presentation 6 – Lea Steele**

**Solvent Exposures in the Gulf War**

---

**Lea Steele, Ph.D.**

**September 19, 2005**

☆☆ RAC-GWVI

**Complex of Chronic Symptoms Described 16 Years after Initial Exposure**

---

- Memory impairment
- Balance problems
- Fatigue
- Headache
- Mood and personality changes
- Neuroimaging studies show abnormalities in some individuals
- Mild mental status abnormalities in some individuals

JW Albers et al (2000) JOEM 42:410; study of 52 railroad workers with long-term occupational exposure to solvents

☆☆ RAC-GWVI

**Syndromes Described Following Chronic Exposure to Organic Solvents**

---

- Solvent-related chronic encephalopathy
- “Painter’s syndrome”
- Chronic solvent encephalopathy variously classified: from less severe (multiple nonspecific symptoms) to very severe (dementia, marked global deterioration)

☆☆ RAC-GWVI

**Solvent Exposures in the Gulf War**

---

- Solvents
  - > Additional broad class of neurotoxins to which Gulf War veterans were exposed
  - > Previous reports have generally looked at solvents as part of exposure groups: neurotoxins, hydrocarbon compounds
  - > Wide use of diverse types of solvents in the Gulf War and generally in the military
  - > Little specific information on use or health effects of solvents in the Gulf War

☆☆ RAC-GWVI

## Solvents

- Thousands of types of diverse chemicals that dissolve/dilute other chemicals
- > Organic solvents: widespread use and exposure
  - > paints and varnishes
  - > cleaning/degreasing
  - > fuels

☆☆ RAC-GWVI

## Solvents Sent to the Gulf War

- Acetic acid
- Acetone
- Amyl acetate
- Benzene
- 2-Butoxyethanol
- Butyl acetate
- Butyl alcohol
- Camphor
- Chloroform
- Cresol
- Cresylic acid
- Cyclohexanol
- Cyclohexane
- Cyclohexanone
- Dichlorodifluoromethane
- Diethylene glycol
- Diethylene glycol monobutyl ether
- Diethylene triamine
- Dipropylene glycol
- Ethanol
- Ethyl acetate
- 2-Ethyl butanol
- Ethylene glycol
- Ethylene glycol monoethyl ether
- Ethylene glycol monomethyl ether
- Ethyl ether
- Glycerol
- n-Heptane
- Hexyl alcohol
- Hexylene glycol
- Isoamyl acetate

Source: Gulf War and Health, Vol.2, Institute of Medicine, 2003

☆☆ RAC-GWVI

## Solvents Sent to the Gulf War, continued

- Isopentyl alcohol
- Isopropyl alcohol
- Methanol
- 1-Methoxy-2-propanol acetate
- Methylene chloride
- Methyl ethyl ketone
- Methyl isoamyl ketone
- Methyl isobutyl ketone
- Methyl propyl ketone
- Morpholine
- Naptha
- Phenol
- Polyalkylene glycol
- Potassium hydroxide
- Propylene glycol
- Stoddard solvent
- Tetrachloroethylene
- Toluene
- 1,1,1- Trichloroethylene
- 1,1,2- Trichloro-1,2,2-trifluoroethane
- Trichloroethylene
- Tricresyl phosphate
- Xylene

Source: Gulf War and Health, Vol.2, Institute of Medicine, 2003

☆☆ RAC-GWVI

## Health effects of solvent exposures

- Mucous membrane/dermal irritation
- CNS effects
- Peripheral neuropathy
- Anemia, leukopenia, thrombocytopenia
- Cancers
- Liver disease
- Renal toxicity
- Reproductive toxicity & teratogenicity

☆☆ RAC-GWVI

### Neurotoxic effects of solvents

---

- Neurological signs:
  - > Cranial nerve abnormalities (e.g. trigeminal neuropathy)
  - > Muscle weakness, incoordination
  - > PNS signs (e.g. insensitivity to pinprick and touch, changes in sensation to position, vibration, temperature)

### Neurotoxic effects of solvents

---

- Neuropsych deficits:
  - > Attentional capacity
  - > Executive function
  - > Visuospatial skills
  - > Short-term memory
  - > Mood/ affect
- Symptoms may resolve upon withdrawal of acute, low-dose exposures
- Chronic exposure may be associated with permanent changes

### Activities Associated with Exposure to Particular Classes of Solvents in the Gulf War

---

- Cleaning/degreasing
- Electronic/radio repair
- Refrigeration servicing
- Vehicle painting
- Vehicle repair

### IOM Review – Possible health effects of solvents identified as present in Gulf War

---

#### Sufficient Evidence of Causal Relationship:

- > Benzene and acute leukemia
- > Benzene and aplastic anemia

#### Sufficient Evidence of an Association:

- > Benzene and adult leukemia
- > Solvents and acute leukemia
- > Propylene glycol and allergic contact dermatitis

### IOM Review – Possible health effects of solvents identified as present in Gulf War

Limited/ Suggestive Evidence of an Association:

- **Cancers:**
  - > Tetrachloethylene, dry-cleaning solvents and bladder cancer
  - > Solvents and bladder cancer
  - > Tetrachloethylene, dry-cleaning solvents and kidney cancer
  - > Benzene and non-Hodgkin's lymphoma
  - > Solvents and multiple myeloma
  - > Solvents and adult leukemia
  - > Solvents and myelodysplastic syndromes

Gulf War and Health: Volume 2: Insecticides and Solvents, IOM, 2003



### IOM Review – Possible health effects of solvents identified as present in Gulf War

Limited/ Suggestive Evidence of an Association:

- **Neurologic Effects:**
  - > Solvents and neurobehavioral effects
- **Other Health Effects:**
  - > Solvents and reactive airways dysfunction syndrome
  - > Solvents and hepatic stenosis
  - > Solvents and chronic glomerulonephritis

Gulf War and Health: Volume 2: Insecticides and Solvents, IOM, 2003



### Epidemiologic Studies: Solvents in the Gulf War How Many Were Exposed?

Study	Population	Exposure		
Iowa Study, 1997	1,896 GW vets	Solvent/ petrochemicals	Reg. military NG/Reserves	88.7% 91.2%
Kang, 2000	11,441 GW vets	Other paint, solvent, petrochemical	All veterans VA Registry	29.7% 53.3%
Unwin, 1999	2,735 UK GW vets	Other paints or solvents		63.9%
Pierce, 2005	495 Air Force female GW vets	Decontamination solutions Refrigeration service Vehicle repair	Avg. # days exposed	17.25 days 7.52 days 13.61 days



### Epidemiologic Studies: Solvents in the Gulf War Association With Health Outcomes

Study	Outcome	Exposure	Findings
Iowa Study, 1997 (1,896 GW vets)	Depression Cognitive dysfunction Fibromyalgia	Solvent/ petrochemical	Prevalence diff, p-value 6.1, p < 0.001 6.6, p < 0.001 4.6, p < 0.001
Kelsall, 2005 (1,424 Austr. GW vets)	Mean # neuro symptoms	Solvents	Adj. ratio of means 1.8 (1.3-2.5)
Reid, 2001 (3,531 UK GW vets)	CFS MCS	Other paints/ solvents	OR = 1.3 (0.8-2.2) unadj OR = 1.4 (0.8-2.5) adj OR = 2.2 (1.1-4.4) unadj OR = 2.4 (1.1-5.1) adj
Unwin, 1999 (2,735 UK GW vets)	CMI	Other paints/ solvents	OR = 1.7 (1.5-2.0) unadj



**Epidemiologic Studies: Solvents in the Gulf War  
 Association With Health Outcomes**

Study	Outcome	Activities in Theater	Findings
Spencer, 2001 (1,119 GW vets)	CMI	Vehicle repair	3.29 (1.38-5.76) unadj
		Battery repair	2.69 (1.32-5.46)
		Generator repair	2.13 (1.16-3.91)
		Refrigerator service	2.88 (0.91-9.13)
		Electrical radio repair	1.16 (0.61-2.22)
		Degreasing machinery	2.37 (1.34 – 4.19)

**Organic Solvents**

- Solvents can have both acute and chronic effects on the CNS
- Specific effects vary with compound; structurally-related compounds can have similar effects
- Exposures often involve mixtures of solvents; little scientific research on effects of mixtures
- In the Gulf War, exposure to most organic solvents was for more limited duration than typically associated with chronic encephalopathy

**Solvents in the Gulf War**

- Widespread exposure (up to 90%) to diverse types of solvents; little information on specific compounds
- Self-reported exposure to “solvents/paints” generally associated with increased rates of symptoms, multisymptom illness (RR~2.0)
- One study indicated that Gulf War occupations associated with greater solvent use have increased rates of CMI (OR ~ 2-3)

**Solvents in the Gulf War**

- As a general class, solvents have generally not been considered primary “suspects” in the etiology of Gulf War illnesses
  - > Multiple types of compounds
  - > Exposures often limited to specific occupational groups
  - > Most solvents to which veterans were exposed not unique to Gulf War deployment
- Little research information on potential for interactive effects with other exposures experienced in the Gulf War
  - e.g., some solvents inhibit AChE in some regions of the brain

### **Solvents: Special Areas of Consideration**

---

- Fuel exposures in the Gulf War
- CARC painting operations

**Presentation 7 – Barbara LaClair**

**Fuel Exposures of U.S. Military During the Persian Gulf War**

---

Barbara LaClair, M.H.A.

Meeting of the Research Advisory Committee  
on Gulf War Veterans' Illnesses  
September 19, 2005

★★ RAC-GWVI

**Fuel Exposures in the Gulf War:**

---

- Variety of fuels used in Gulf War – mostly jet fuel
- Jet fuel used in most military vehicles, including tanks and trucks
- One of the most widespread exposures during the War
- Jet fuel exposure associated with variety of toxic effects

★★ RAC-GWVI

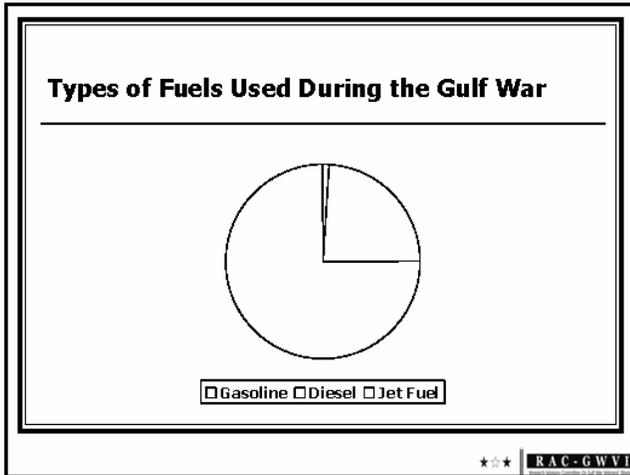


**Fuel is vital to military operations**

---

- 1.88 *billion* gallons of fuel used by U.S. military operations in ODS/S between August 10, 1990 and May 31, 1991
- Fuel Uses:
  - > Vehicles, aircraft, equipment
  - > Tent heaters, cooking stoves, portable generators
  - > Dust & sand suppression
  - > Fuels as solvents
  - > Burning trash and wastes

★★ RAC-GWVI



- ### Types of Fuels Used During the Gulf War
- Jet fuels, kerosene (Jet A-1, JP8, JP4, JP5) (75%)
    - > Jet A-1 - Commercial fuel, primarily kerosene
    - > JP-8 - Military version, Jet A-1 with additives
    - > JP-4 - Kerosene/gasoline mix, being phased out in 1991
    - > JP-5 - Primarily kerosene, Navy's primary jet fuel
  - Diesel fuel (24%)
  - Gasoline (leaded) (1%)
- Fuels obtained from local sources - primarily from Saudi Arabia
- \*\*\* RAC-GWVI

- ### DoD Single Fuel Policy
- Adopted March 1988, in scheduled phase-in at start of ODS
  - Goal - Reduce support requirements and maximize efficiency, by:
    - > Minimizing number of different fuels required
    - > Taking maximum advantage of locally available fuel
  - JP-8 designated as primary fuel for air and ground forces
- \*\*\* RAC-GWVI

- ### JP-8 was used in....
- Aircraft (land-based)
  - Helicopters
  - Abrams Tanks
  - Bradley Fighting Vehicles
  - HumVees
  - Heavy trucks
- \*\*\* RAC-GWVI



Fuel handling personnel moving fuel lines, 101st Airborne Division Rapid Refuel Point

### JP-8 as the Fuel of Choice

- Replaced JP-4
- Similar to commercial Jet A-1, with additives
  - > Static dissipator
  - > Corrosion inhibitor
  - > Icing inhibitor
- Contains less benzene (carcinogen)
- Contains less n-hexane (neurotoxicant)
- Thicker, less volatile
  - > Reduced risk of fires, explosions



Fuel handling personnel and M-978 tanker, 18th Aviation Brigade



Incineration of human wastes

### Dust and Sand Suppression during the Gulf War

- “He described one brigade dumping 30,000 gallons of diesel fuel on the roads daily, and said U.S. service members living in tents near the roads and particularly truck drivers carrying out the spraying- complained of nausea from breathing the resulting fumes. As a result, the preventive medicine person to whom they reported obtained respirators for the drivers’ use.”

-- testimony of D. Johnson, U.S. Army Sanitary Engineer, to the NIH Technology Assessment Panel in 1994, as summarized in the Presidential Advisory Committee on Gulf War Veterans’ Illnesses, Final Report, December 1996.

### Dust and Sand Suppression during the Gulf War

- “During the Persian Gulf War, JP-8 was routinely used to control and suppress desert sand, and combusted JP-8 was used to obscure troops and equipment. With desert surface temperatures commonly exceeding 120°F, substantial exposure may have occurred as a result of vaporization of JP-8. When vaporized jet fuel mixes with wind-blown ultrafine desert sand particles, pulmonary exposure is highly possible”

— *Toxicologic Assessment of Jet-Propulsion Fuel 8*, National Research Council, Subcommittee on Jet-Propulsion Fuel 8, Committee on Toxicology, National Academies Press, 2003

### Fuels used for dust suppression

“Because there is the potential for substantial exposure of troops to JP-8 when it is used to suppress desert sand and as a method of obscuring troops and equipment, the subcommittee recommends that the DOD no longer use JP-8 for those purposes”

- *Toxicologic Assessment of Jet-Propulsion Fuel 8*, National Research Council, Subcommittee on Jet-Propulsion Fuel 8, Committee on Toxicology, National Academies Press, 2003

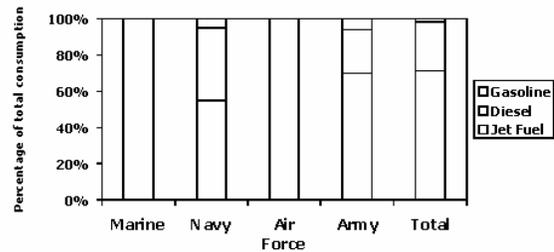
### Types of fuels used varied...

- By branch of service,
- By unit,
- Over time

### DoD Single Fuel Policy - Implementation Issues

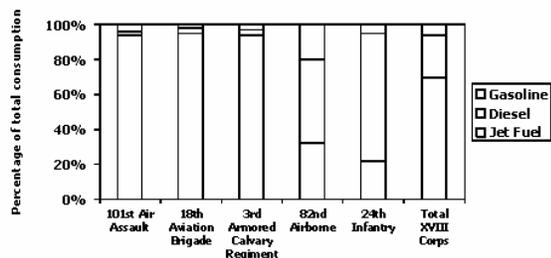
- > Some Air Force units located on bases where only JP-4 available
- > Army requested permission to use diesel fuel in ground equipment, to support generating smoke for tactical operations in M-1 tank, Abrams and Bradley vehicles
- > Some Army & Marine units experienced power-related problems with ground vehicles, and attributed them to use of jet fuel
- > Problems with fuel filters and injectors becoming clogged

### Fuel Consumption During ODS/S, by Branch of Service



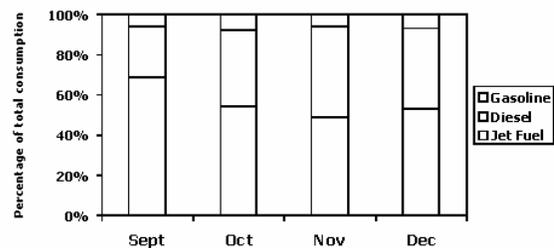
Source: RAMP, Assessment of DoD Fuel Standardization Policies, 1994

### ODS/S Fuel Consumption, XVIII Corps, by Division



Source: RAMP, Assessment of DoD Fuel Standardization Policies, 1994

### ODS/S Fuel Consumption, XVIII Corps, Late 1990



Source: RAMP, Assessment of DoD Fuel Standardization Policies, 1994

## Health Effects of Fuel Exposures

---

☆☆ RAC-GWVI

## Routes of exposure to fuels

---

- Inhalation
  - > Vapors
  - > Aerosols
  - > Combustion products
- Dermal absorption
- Ingestion

☆☆ RAC-GWVI

## JP-8 : Health symptoms reported

---

- Nausea
- Headaches
- Dizziness, lightheadedness
- Fatigue
- Blocked nasal passages
- Respiratory distress
- Skin irritation
- Smelling/ tasting JP-8 hours after exposure

☆☆ RAC-GWVI

## Health Effects – JP-8 exposures

---

- Dermal effects
  - > Irritation, rashes
  - > Altered permeability to other substances
- Pulmonary effects
- Neurobehavioral changes
- Immune effects

☆☆ RAC-GWVI

### JP-8 – Health effects of combined exposures

- **Combined exposure to DEET, PB and JP-8 (in mice)**
  - > Fuel does not profoundly alter many immunological endpoints, but does selectively target functional endpoints
  - > Suppression of antibody-specific IgM immune response (plaque-forming cell)
  - > Decrease in delayed type hypersensitivity following high-dose exposure
- Peden-Adams M, Eudaly J, Eudaly E, et al., Toxicology and Industrial Health 17:192-209 (2001)

### IOM Review - Health effects of exposures to fuels

- Review of over 800 peer-reviewed epidemiologic studies of human health effects of exposures to fuels, combustion products, and propellants
- **Conclusion: Insufficient evidence of association between exposures to uncombusted fuels and any health outcomes evaluated**

- Gulf War & Health, Volume 3: Fuels, Combustion Products and Propellants, Institute of Medicine, 2005

### Epidemiologic Studies of Fuel Exposures in Gulf War Veterans

#### Fuel and petrochemicals – fumes, odors: How many were exposed?

Study	Population	Exposure	
Kang, 2000	11,441 Gulf War vets	Diesel, kerosene or other petrol fumes, incl. tent heaters, vehicle exhaust	80.4%
Unwin, 1999	3,284 UK Gulf War vets	Diesel or petrochemical fumes	84.0%
Wolfe, 2002	945 GW vets, Ft. Devens cohort	Diesel fuel odor	64.5%

**Fuel and petrochemicals – Skin/ dermal exposures:  
 How Many Were Exposed?**

Study	Population	Exposure	
Kang, 2000	11,441 Gulf War Vets	Skin exposure to diesel or other petrochemical fuel	56.6%
McCaughey, 1999	305 Gulf War Vets from OR, WA	Skin contact with petrol fuel	51.0%
Unwin, 1999	3,294 U.K. Gulf War vets	Diesel or petrochemical on skin	66.6%
Australian Study, 2003	1,456 Australian Gulf War Vets	Solvents, oils, diesel or other fuel on skin	78.9%

☆☆ RAC-GWVI

**Exposure to Fuels:  
 Association with symptoms**

Study	Outcome	Exposure	Findings
Suadani, 1999 (667 Danish GW vets)	Neuropsych sympt: memory, headache, dizziness, fatigue, sleep	Diesel, kerosene, other fumes	bivariate association with # symptoms $p \leq 0.01$
		Evap. diesel on ground & dust	$p \leq 0.01$
		Dermal contact, diesel & other	$p \leq 0.001$
		Bathing, drinking contain water (fuel, oil, chem)	bivariate association $p \leq 0.001$ , OR = 2.9 (1.8-4.6) in multivariate model
		Ingest contain food, fumes, oil, chem	$p \leq 0.001$

☆☆ RAC-GWVI

**Exposure to Fuels:  
 Association with symptom complexes**

Study	Outcome	Exposure	Findings
Gray, 2002 (11,868 Seabees)	GWV	oil sprayed for dust control	OR = 2.20 (1.85-2.60) (unadj) OR = 1.16 (0.92-1.46) (saturated)
Spencer, 2001 (1,119 ORMA vets)	CMI	contact with fuel	OR = 3.76 (1.99-7.12) (unadj)
Unwin, 1999 (3,294 UK vets)	CMI	diesel & petro fumes	OR = 2.1 (1.7-2.5) (unadj)
		diesel & petro on skin	OR = 1.8 (1.5-2.1) (unadj)
Reid, 2001 (3,531 UK GW vets)	CFS HCS	diesel on skin	OR = 1.8 (1.8-3.9) OR = 1.7 (0.8-3.6)
Wolfe, 2002 (945 Army vets)	CMI	diesel fuel odor	OR = 2.7 (1.9-3.9) (unadj)

☆☆ RAC-GWVI

**Exposure to Fuels:  
 Association with symptom complexes**

Study	Outcome	Exposure	Findings
Haley, 1997 (249 GW vets)	3 syndromes derived by factor analysis: 1-impaired cognition 2- confusion-ataxia 3- arthro-myo-neuropathy	worked on and sprayed w/ petro.  drinking water had petro. taste	Syndrome 1 RR = 1.8 (0.6-5.6) Syndrome 2 RR = 2.1 (0.9-4.9) Syndrome 3 RR = 0.9 (0.4 - 2.0)  Syndrome 1 RR = 2.6 (0.9-7.7) Syndrome 2 RR = 2.8 (1.3-6.3) Syndrome 3 RR = 2.6 (1.2-5.6)

☆☆ RAC-GWVI

### Summary of Fuel Exposures

---

- Fuel exposures during the Gulf War were common and widespread
- Jet fuels (A-1 and JP-8) were the most widely utilized fuel types; use included ground vehicles and tanks
- Little objective data on fuel exposures – self-report, questions non-specific or ask about multiple exposure types

### Summary of Fuel Exposure Information from Gulf War Studies

---

- ~ 65 – 80% of Gulf War vets report exposure to petrochemical fumes, odors, or exhausts
- ~ 50 – 60% report dermal exposure to fuels, petroleum products

### Summary of Health Outcome Findings from Gulf War Studies

---

- Fuel exposures associated with chronic multi-symptom illness (ORs 1.8-3.8)
- Jet fuel: limited information from Gulf veteran epidemiologic studies

### Speakers : Health Effects of Jet Fuel Exposure

---

Effects on the Immune System      Dr. Mark Whitten

Neurological and Behavioral Effects      Dr. Glenn Ritchie

**Presentation 8 – Glenn Ritchie**

**Possible Role of  
Hydrocarbon Fuel  
Exposures on  
Development of Gulf War  
Illnesses**

**Glenn D. Ritchie, Ph.D.**  
ritchieg@battelle.org  
Group Leader, CNS Safety Pharmacology  
*Battelle-Columbus (OH)*

**Qualifications**

- ❑ 10 years-Assistant Director of the Navy Neurobehavioral Effects Laboratory, Wright-Patterson AFB, OH.
- ❑ First animal study of Gulf War /jet fuel "synergism".
- ❑ 2 major reviews of hydrocarbon fuel toxicity.
- ❑ A number of "fuel" neurobehavioral effects publications.
- ❑ Neurobehavioral research in USAF 7-Base human study
- ❑ Former Navy "expert" for hydrocarbon fuel toxicity.
- ❑ Invited presentations to JANNEF and International Jet Fuel Toxicity Conferences.
- ❑ Member, USAF JP-8 Research Consortium.
- ❑ Navy expert for the Fallon "Angels" leukemia cluster.
- ❑ Involved in the Sierra Vista, AZ cluster investigation.

**Presentation Objectives**

1. Define the different hydrocarbons present in the Persian Gulf theater.
2. Discuss warfighter routes of exposure and hydrocarbon fuel exposure scenarios.
3. Briefly discuss direct health effects of repeated fuel exposures.
4. Provide data on hydrocarbon health effects additivity & synergism with other PGW toxicants.

**Overall Objective**

**To provide evidence that repeated hydrocarbon exposures can (additively or synergistically) increase the effects of exposure to other "military" theater toxicants, and possibly contribute to induction of Persian Gulf illnesses.**

### **Caveats**

1. Clearly, human effects of hydrocarbon exposures appear limited to “minor” CNS, dermal, lung, blood, reproductive, kidney, liver and immune system deficits.
2. Millions exposed repeatedly to hydrocarbon fuels do not become seriously ill.

– but –

Exposure to hydrocarbon fuels and “unique” chemicals and environments may result in illnesses unpredicted by exposure to other Persian Gulf toxicants

## **Hydrocarbons Present in the Persian Gulf**

### **Hydrocarbons Present in the Persian Gulf**

- JP-8 (USAF & US Army) – JP8 (100)??**
- JP-5 (US Navy)**
- JP-4 (Turkey, Saudi Arabia & other Allies)**
- Kerosene**
- Diesel and Marine Diesel**
- Limited AVGAS & Gasoline**
- Numerous Lubricants & Solvents**
- Large Quantities of Fuel Additives**
- Jet-A, AVGAS, gasoline**
- Jet Oils (tricresyl phosphate)**

### **What is JP-8?**

- 220 hydrocarbons; 2000+ isomeric forms.
- Complex mixtures of aliphatic, aromatic and substituted naphthalene hydrocarbons (C4-C22).
- Benzene, methylbenzenes, ethylbenzenes, cyclohexylbenzenes.
- Xylenes.
- Toluene.
- Naphthalenes.
- Known and proprietary fuel additives that may contain BHT, DIEGME (diethylene monomethyl ether), xylenes, toluene and benzene.

### **Predicting the “Toxicity” of Hydrocarbon Fuels**

- Each hydrocarbon fuel has a unique “hydrocarbon cut” and additive package.
- Fuels produced by different refineries are substantially different in chemical content.
- Each new iteration of jet fuel is less volatile than the previous version, increasing dermal exposure potential.
- Volatile hydrocarbons removed from fuels to reduce toxicity are replaced with proprietary additives that may contain similar toxicants.
- For example, Kuwaiti crude oil is very different from crude oil in the US.

### **Routes of Exposure and Hydrocarbon Fuel Exposure Scenarios**

#### **Routes of Exposure**

- Inhalation of fuel vapor.**
- Inhalation of fuel aerosol (vapor/aerosol).**
- Inhalation of sand aerosols.**
- Inhalation of combusted hydrocarbons.**
- Direct dermal exposure to neat fuels.**
- “Second-hand” exposure to contaminated clothing (family).**
- Hydrocarbons mixed in drinking or shower water.**
- Hydrocarbons mixed in food.**

#### **Exposure Scenarios**

##### **Neat fuels – conventional scenarios**

- Fuel transportation (truck, aircraft and pipeline).
- Fuel handling.
- Fuel storage .
- Fueling of aircraft, land craft, equipment, heaters.
- Fuel related to vehicle/aircraft operation.

“Presence at any location where fuels were used.”

## Exposure Scenarios

### Neat Fuels – unconventional scenarios

- Cold start-up of aircraft (up to 10% raw fuel released).
- Numerous fuel spills & leaks.
- Equipment, munitions and vehicle cleaning with fuels.
- Use in vented / unvented tent heaters.
- Vehicle-delivered sand suppression using fuels.
- Aircraft-delivered sand suppression using fuels.
- Kuwaiti oil fires (?% uncombusted oil).
- Aircraft fuel tank upper atmosphere “dumping”.
- Use of JP-8 in cooling systems.
- Smoke screen (obscurant) generation.
- “Apple Jelly” containing LPS (C8-C10 fractions).

## Hydrocarbon Combustion Byproducts

- Neat fuel (up to 10%)
- Up to 30 polycyclic aromatic hydrocarbons (PAHs), many of which are known carcinogens.
- Carbon monoxide
- NO<sub>x</sub>
- Formaldehyde
- SO<sub>x</sub>
- Extensive respirable particulates

## Direct Health Effects of Repeated Hydrocarbon Exposures

## CNS Effects of Fuel Exposures

- Severe psychiatric symptoms; neurasthenia; polyneuropathy; shortened attention span; EEG alteration; reduced auditory evoked cortical potentials (Knave and associates, 1976-1980).
- Increased human postural sway (Smith et al., 1997).
- Human exposed chronically (National Guard) exhibited significantly poorer performance of 20/47 NeuroCog Battery measures (Mitchell, Kay and Risby, 2004; Anger et al.).
- Jet fuelers were impaired on acquisition of classically conditioned eyeblink response (Bekkedal, Rossi & Ritchie).
- Hearing impairment (synergistic fuel x noise) [Kaufman et al., 2005]. Gene expression changes related to CNS neurotransmitter signaling pathways (Lin, Ritchie et al., 2004).



### **CNS Effects of Fuel Exposure**

- Rats were exposed by whole body inhalation to 1000 mg/kg (H), 500 mg/kg (L) or 0 mg/kg (C) JP-8 vapor for 6 h/d, 5 d/w, for 6 w. (Ritchie et al., 2001).
- After 65-d rest, rats (n = 15) were trained on simple, moderate difficulty, and complex operant tasks.
- All learned simple tasks equally well; low-dose learned moderate difficulty tasks slightly better than high dose; the high dose group was greatly impaired on learning the complex task (IRA, incremental repeated acquisition) compared to controls or the low dose group.

### **Dermal Toxicity**

- One of the major complaints of military fuel workers is chronic dermatitis (increased ROS). (Riviere, McDougal).
- Dermal absorption is related to carbon chain length (mild irritation to skin cancer) and exposure duration.
- JP-8 induces dermal irritancy: erythema, epidermal edema, increased epidermal thickness, subcorneal microabscesses, and dermal microlesions/lesions.
- Induction of proinflammatory cytokines (IL-1-alpha, TNF-alpha, IL-8).
- Lipid extraction from the stratum corneum.
- Dermal exposure to JP-8 resulted in significant changes in protein expression in 35/929 dermal proteins surveyed (Witzmann et al., 2005).

### **Immune & Blood Effects**

- Keil et al. (2004) (mice, 14 days, JP-8 gavage)-reduced hematocrit, hemoglobin concentration, and red blood cell count; increased liver mass; decreased thymic cellularity; alterations in splenic CD4/8 subpopulations with high dose gavage.
- Reduced thymus weight and immune cell populations in thymus; decreased immune function as identified by mitogenesis assays (Harris et al., 2001 - dermal application).
- Blood and bone marrow genotoxicity (micronuclei) [Vijayalaxmi et al., 2004 – vapor / aerosol exposure).
- (Respiratory) Natural Killer (NK) cell function was nearly eliminated, and lymphokine-activated killer cell activity was suppressed (Harris et al., 2000).

### **Immune & Blood Effects**

- Five minimal applications, or one large dermal application of JP-8 induced immunosuppression in mice (Ullrich, 1999).
- Contact hypersensitivity to a bacterial antigen was significantly suppressed.
- The ability of splenic T lymphocytes to proliferate was suppressed.
- IL-10, a potent immunosuppressive cytokine, was found in serum
- JP-8 (100) > JP-8 > JP-4 in inducing genotoxicity in peripheral lymphocytes (Jackman et al., 2002 – cell cultures).

### **Pulmonary Toxicity**

- Increased lung compliance (Pfaff et al., 1995).
- Increased lung epithelial permeability (Hays et al., 1995).
- Decreased BALF concentrations of Substance P (Witten et al.).
- Increased protein levels in BALF (Robledo et al., 2000).
- Secretion of IL-1-beta, IL-6, Tumor Necrosis Factor (TNF)-alpha.
- Apoptosis in lung epithelial cells (Stoica et al., 2001).
- Dose-related protein up regulation (30 at 2500 mg/m<sup>3</sup>) and down regulation (135 at 2500 mg/m<sup>3</sup>) [Drake, Witzmann et al., 2003].

### **Additional Toxicity**

- Minimal evidence of hepatotoxicity (Witzmann et al.)
- Limited effects on male and female reproductive systems (LeMasters and Colleagues; Witzmann et al.).
- Renal toxicity that seems limited to rodent species (Mattie and Colleagues; Witzmann et al.)

### **Additivity and Synergism Data Related to Hydrocarbon Exposures**

### **Major Exposure Co-Factors**

- Physiological / psychological stress
- PB and/or atropine
- DEET, Permethrin & 63 other pesticide treatments
- Tungsten, DU & lead munitions
- Aerosolized DU and W
- Desert environment – heat/cold
- Sand aerosols
- Numerous hydrocarbon solvents, cleaners
- Low-level sarin (sulfur mustard?) exposures
- Anti-war gas treatments (PB and atropine)
- Population mixing
- Known and unidentified vaccinations
- Endogenous parasites and infections
- Sewage and water quality

## Desert Aerosols

- Persian Gulf sand varies by location, and contains respirable and non-respirable particles.
- Frequent winds and vehicle movements result in “sand aerosols”
- Toxicants in the sand can become attached to respirable and non-respirable particles that enter the lungs
  - Dumped and spilled fuels
  - Depleted tungsten, DU and lead munitions
  - Animal (bird) wastes
  - Human wastes

## Persian Gulf Study (1994)

- Male S-D rats were exposed for 6/hr day for 14 days to:**
  - JP-4 vapor (1000 mg/kg)
  - Unpredicted footshock stress
  - DEET (shaved skin/acetone) & PB (corn oil)
- Half were rested 14 days, then tested**
- Half were rested 60 days, then tested**
- Eight neurobehavioral tests (all animals)**
- Neurotransmitter levels in 4 brain areas**

## Persian Gulf Study (1994)

- Exposure scenarios:**
  - Control (C):** Room Air, Corn Oil, Acetone
  - Vapor (V):** JP-4 vapor
  - Stress (S):** Unpredicted footshock
  - PB & DEET (PB&D):** PB in corn oil (gavage) and DEET in acetone (dermal to shaved skin)
  - Treatment Groups:** C, V only, S only, PB&D only, V/S, V/PB&D, S/PB&D, V/S/PB&D

## Persian Gulf Study Results

- JP-4/S decreased grip strength (14-d); stress increased grip (60-d).** 
- JP-4 increased ARAS (14-d); stress/PB&D increased ARAS (60-d).**
- Stress, JP-4/Stress and Stress/PB&D, decreased acoustic startle response (14-d).** 

## Persian Gulf Study Results

□ **JP-4 or stress/PB&D decreased prepulse inhibition (60-d).**



□ **JP-4 decreased total locomotor activity (60-d).**



□ **JP-4, stress, or stress/PB&D decreased tail flick latency (60-d).**



## CNS Neurotransmitters

CNS neurotransmitter levels are modulated by JP-4 or JP-5 inhalation exposures (measured as long as 80+ days post-exposure) (Nordholm et al, 1999; Ritchie et al., 2001):

- Depleted dopamine (DA).
- Elevated DA metabolite dihydroxyphenylacetic acid (DOPAC).
- Elevated serotonin (5-HT).
- Increased 5-HT metabolite homovanillic acid (HVA).
- Increased 5-HT metabolite 5-hydroxyindoleacetic acid (5-HIAA).

## Fuel Synergism

□ A number of human metabolic interactions have been identified among chlorpyrifos, carbaryl, DEET, permethrin, PB, solvent and jet fuel exposures.

□ **Permethrin** has been shown inhibit the metabolism of DEET (cytochrome P450) and carbaryl (Hodgson and Rose, 2005).

□ **JP-8** has been shown to inhibit CYP 1A2 and 2B6 metabolism of DEET (Edwards et al., 2005).

## Synergism Studies

□ Riviere et al., 2002.

□ Isolated porine skin flap (soaked fabric occlusion).

□ Low level sulfur mustard, JP-8 + DEET on transdermal absorption of permethrin.

□ Normally DEET or sulfur mustard inhibits permethrin dermal absorption.

□ JP-8 increased permethrin percutaneous absorption (2x) and skin penetration (3x).

## Antioxidant Effects

- JP-8 induces generation of reactive oxygen species (ROS).
- JP-8 significantly depletes intracellular glutathione stimulating hormone (GSH) (Smulson et al, 2002).
- Aerosolized JP-8 reduced glutathione-S-transferase (GST) in the retina (McGuire et al., 2000).

## Fuel Synergism

- Fuel exposure radically alters dermal and pulmonary system permeability to other potential toxicants.
- Fuel exposure suppresses the immune system.
- Hydrocarbon exposures suppress normal xenobiotic metabolism systems.
- Fuels may increase generation of Reactive Oxygen Species.
- Fuel may interact synergistically with heavy metals (i.e., W, Arsenic, DU) to induce blood-related cancers.

## The Fallon “Angels”

- **Fallon, NV (24,000 residents & military)**
- **Desert environment**
- **Much JP-8 use, leaking, dumping**
- **Top Gun relocated to Fallon NAS by 1998**
- **40,000 sorties/year**
- **Lead, DU and W munitions**
- **Highest arsenic (in water) in the world**
- **Tungsten mining/ smelting (in water, air, trees)**
- **1963 underground nuclear test**
- **Population mixing**

## Sierra Vista Cluster

- **Sierra Vista, AZ (28,000)**
- **Desert environment**
- **Ft. Huachuca (unmanned drones)**
- **Numerous “touch-downs”/year**
- **JP-8 / AVGas / Combustion Byproducts**
- **High arsenic (in air)**
- **Tungsten in water, air, trees**
- **Mexican Garbage Fires – Local Wildfires**
- **Mexican Cu Smelting**

### **The Fallon “Angels” and Sierra Vista Equation**

**Desert + Military Base + High Heavy Metals**

**As many as 17 cases of Acute Lymphocytic  
Leukemia (ALL) and Unexplained High  
Rates of Adult Cancers (cluster should  
occur by chance in US once every 22,000  
years)**

### **The Persian Gulf**

- **Desert environment**
- **Military “bases”**
- **Extensive exposure to hydrocarbons**
- **Lead, DU, W munitions**
- **High physical/psychological stress**
- **Population mixing**

### **Summary**

- Warfighters in the Persian Gulf were/are repeated exposed, through multiple routes, to a wide diversity of hydrocarbons, as well as to numerous other toxicants.
- Repeated exposure to hydrocarbons is known to induce direct health effects in at least the CNS, skin, lungs, immune system, and blood.
- JP-8 can increase dermal and pulmonary absorption of xenobiotics, reduce metabolism of xenobiotics, reduce immune function, and increase levels of ROS.

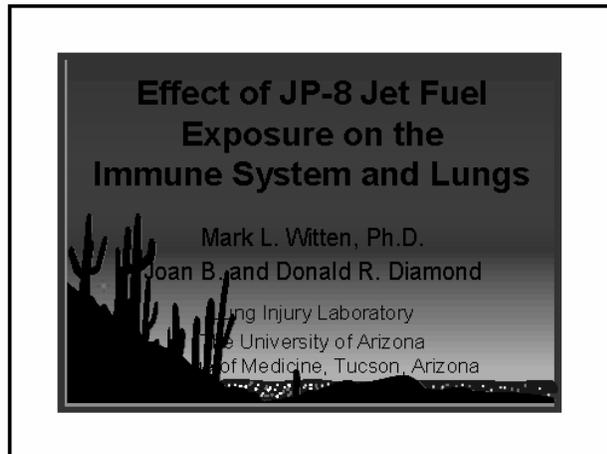
### **Summary**

**It appears logical to assume that  
concurrent exposure to  
hydrocarbon fuels and other  
diverse “military theater”  
toxicants could induce health  
effects in at least susceptible  
individuals that might not  
otherwise occur.**

## **Research Plan**

- **Rats and/or monkeys**
- **Whole body exposures**
- **6 hr/day for 30 days**
- **Permethrin x DEET x JP-8 x Stress x Sand x Heat**
  - Permethrin at normal human dermal dose
  - DEET at normal human dermal dose
  - Stress = unpredicted foot shock
  - JP-8 vapor/aerosol mixture & dermal exposure
  - Sand aerosol
  - 100 °F

**Presentation 9 – Mark Witten**

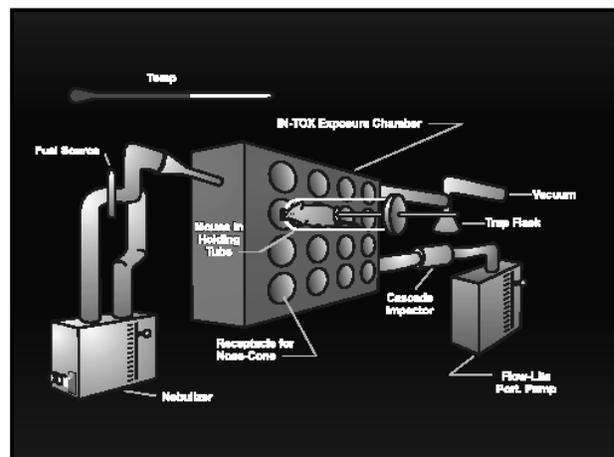


### Gulf War Illnesses Syndrome

- Visit to Saudi Arabia in June of 1995
- Talks with Saudi health officials
- Extent of air pollution from Kuwait oil fires
- Personal experiences of my cousin during Gulf War 1

***My talk will be divided into three segments***

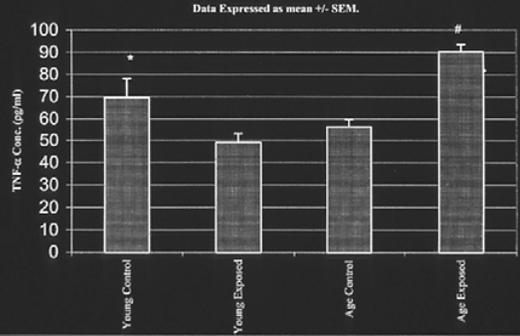
- Lung Immune Data
- Systemic Immune Data
- Skin Immune Data



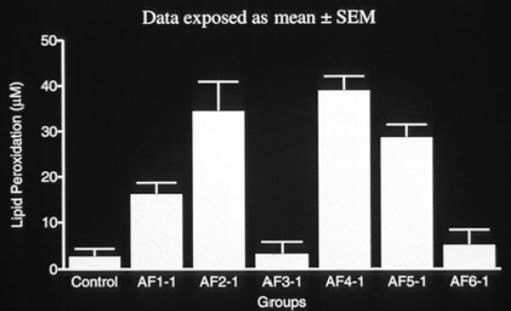
### Age-Related Differences in Pulmonary Inflammation to JP-8 Jet Fuel Aerosol Inhalation

- C57BL/6 mice split into a young (3.5 month old) group and adult (12 months old) group.
- JP-8 jet fuel exposure at 1000 mg/m<sup>3</sup>/hr for 7 days.
- JP-8 exposed young and adult mice had similar responses with regards to lung dynamic compliance, lung permeability, BALF cell count, and decreased PGE<sub>2</sub>.
- Total lung cell counts in both the adult (<33%) and young (<50%) JP-8 jet fuel-exposed mice compared to controls. However, % PAM < in the adult mice while remained stable in the young mice.
- TNF $\alpha$  and 8-iso- PGF<sub>2</sub> $\alpha$  responses varied between the adult vs. young mice.

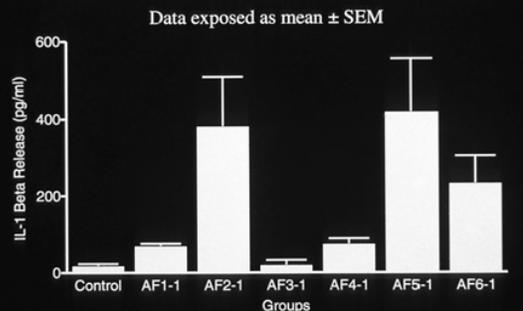
Tumor Necrosis Factor-alpha (TNF- $\alpha$ ) Release From Lungs Of Mice Exposed To Seven Days JP-8 Blend Jet Fuel.



Lipid Peroxidation from Alveolar Type II Epithelial Cells Exposed to AF Particulates



IL-1 Beta Release from Alveolar Type II Epithelial Cells Exposed to AF Particulates



### Immune System

- JP-8 jet fuel exposure for one hour/day
- 100mg/m<sup>3</sup> conc – Decrease in cellularity of the thymus.
- 500mc/m<sup>3</sup> conc – Decreased spleen weight and cellularity.
- 1000 mg/m<sup>3</sup> conc – Decreased ability of spleen cells to mediate immune responses.

- Adult Female B6C3F1 mice given JP-8 (olive oil carrier) by gavage ranging from 250-2500 mg/kg/day for 14 days.
- Thymus mass < at exposure levels  $\geq 1500$  mg/kg/day.
- Decreases in thymic cellularity were observed at exposure levels of 2000 mg/kg/day.

- Decreases in plaque – forming cell response were dose responsive at levels of 500 mg/kg/day.
- Alterations were detected in thymic and splenic CD4/8 subpopulations.
- Proliferative responses of bone marrow progenitor cells were enhanced in mice exposed to 2000 mg/kg/day of JP-8

### Key Point

Humoral immune function is impaired with lower concentration of JP-8 than is required to affect primary and secondary immune organ weights and cellularity, CD4/8 subpopulations, and hematological endpoints.

**JP-8 Jet Fuel Exposure of  
1000 Mg/M By Female C57BL/6 Mice  
For One Day**

- Decrease in thymus cellularity
- Decrease in spleen cellularity, but not as pronounced as thymus.
- Spleen immune cells associated with apoptosis (CD4/8, Mac 1, CD45R) were increased, Dec-205 was decreased and CD-16 was unchanged at one day post – exposure to JP-8.

Cytokines IFN gamma, IL-4, and IL-10 associated with CD4/8 and Mac-1 cells were increased at days +1 and +4 after JP-8 exposure.

**Dermal Immune Responses**

- Low (50 µl/day) JP-8 jet fuel administration of five consecutive days in C3H/HeN mice suppressed contact and delayed hypersensitivity responses, including depressing the protective effect of prior vaccinations.
- Hypothesis – IL-10 and PGE2 are produced by keratinocytes that distribute through the systemic circulation and down-regulate the cell-mediated immune response.

**JP-8 Dermal Exposure for  
4 Hours**

- Increases in TNF and IL-8 in human keratinocytes.
- This is the same time-frame observed in rats for IL-1 and inducible nitrous oxide synthetase.

### **Potential Mechanism for JP-8 to Induce Keratinocyte Cell Necrosis**

High intrinsic levels of Bcl-2 and Bcl-x(L) may prevent apoptotic death of keratinocytes at lower levels of JP-8 jet fuel exposure while perturbation of the balance between pro-and antiapoptotic Bcl-2 family members at higher levels may induce necrotic cell death in human keratinocytes.

### **Conclusions**

- JP-8 jet fuel is a toxic substance.
- Demonstrated immune system effects at levels of JP-8 as low as 100 mg/m.
- There are age related effects to the JP-8 response.
- Dermal exposure may have body wide immune system perturbations.

**Presentation 10 – Lea Steele**

**Additional Exposures of Possible Concern in Relation to the Health of Gulf War Veterans**

---

**Lea Steele, Ph.D.**

September 20, 2005

\*\*\* RAC-GWVI

**Additional Exposures Potentially Associated with Adverse Health Effects**

---

- Microwaves/electromagnetic radiation
- Contaminated food and water
- Decontaminating agents
- CARC Paint

\*\*\* RAC-GWVI

**Additional Exposures**

---

- *Most affect smaller subset of veterans*
- *Not clear what chronic health effects might be*
- *Tend to not have little data or specific information on either exposures or health effects*

\*\*\* RAC-GWVI

**Microwaves/  
Electromagnetic Radiation**

---

\*\*\* RAC-GWVI

**Electromagnetic Radiation**

---

Sources:

- Communications Equipment
  - > Microwave towers
  - > Radios
- Energy beam weapons being developed/tested in 1990-1991 Gulf War

☆☆ RAC-GWVI

**Self-Reported Exposures to Electromagnetic and Microwave Radiation**

Study	Population	Exposure		
Kang, 2000	11,441 GW vets	microwaves	All veterans	23.7%
Kronke, 1996	18,495 CCEP registrants	microwaves		33.0%
Pierce, 2005	495 female GW vets	Electromagnetic radiation	Avg. # days exposed =	43.61
Stuart, 2002	54,244 GW Vets, CCEP partic.	microwaves	Male	18.3%
			Female	23.5%
Combined Analysis	21,306 VA registrants	microwaves		33%

☆☆ RAC-GWVI

**Electromagnetic Radiation**

---

Summary:

- Exposure reported by 20-30% of surveyed veterans
- No data on health effects
- Potential association with Gulf War illnesses?

☆☆ RAC-GWVI

**Contaminated Food and Water**

---

☆☆ RAC-GWVI

### Contaminated Food and Water

---

- Government reports suggest nearly all food and water was supplied by the military
- Food poisoning events in camps commonly reported by veterans

★★★ RAC-GWVI

### Government Reports Suggest Nearly All Food Was Supplied by the Military

---

- “ All food DOD military and civilian personnel consumed was provided by the military in the form of meals ready to eat (MREs) or provided in mess halls. Large numbers of meals were not eaten on the local economy and there was no reason to believe that the local food was contaminated with oil fire residue.”

---- Environmental Surveillance Health Risk Assessment, Kuwait Oil Fires, CHPPM, 1998

★★★ RAC-GWVI

### Contaminated Food and Water: Government Reports Suggest Water Was all Bottled or From Clean Military Tankers

---

- “DOD military and civilian personnel were provided with sealed containers of bottled water for their consumption. Local drinking water supplies were not utilized. Drinking water was therefore considered a safe, uncontaminated media...”

---- Environmental Surveillance Health Risk Assessment, Kuwait Oil Fires, CHPPM, 1998

★★★ RAC-GWVI

### Exposures to Contaminated Water OSAGWI 2000 Report

---

- While the overall result of water operations during ODS/S was a reliable supply of water fit for consumption, there were exceptions:
  - U.S. supplies of non-potable water were occasionally used for food preparation and drinking
  - A number of units were forced to rely on host nation water delivered by tankers
  - Field Manual 10-280, in effect during ODS allowed use of petroleum transport tankers to carry water, once tanks super-chlorinated and flushed thoroughly

--- DOD, Close-out Report: Water Use, 2000

★★★ RAC-GWVI

**Epidemiologic Studies: Local or Contaminated Food  
 How Many Were Exposed?**

Study	Population	Exposure	
Kang, 2002	11,441 GW vets	Ate local non-military food	All vets 74.9%
		Ate food contam w/ smoke, oil, chem	All vets 30.2%
Kronk, 1998	18,495 CCEP registrants	Non-US foods	66.0%
		Contaminated foods	21.0%
McCauley, 1999	305 GW vets	Ate local foods	74.0%

☆☆ RAC-GWVI

**Epidemiologic Studies: Local or Contaminated Food  
 How Many Were Exposed?**

Study	Population	Exposure	
Pierce, 2005	495 AF female GW vets	Contaminated food or water	Avg. # days exposed 24.75 days
		Local, non-AF food	57.09 days
Reid, 2001	3,531 UK GW vets	Local food	20.6%
Unwin, 1999	2,735 UK GW vets	Local food	69.4%
VA Registry		Ate non-US food	71.3%
		Ate contaminated food	33.2%

☆☆ RAC-GWVI

**Epidemiologic Studies: Contaminated Food  
 Associations with Health Outcomes**

Study	Outcome	Exposure	Findings
Boyd, 2003 (678 GW registry vets w/GWV)	Mean factor scale score	Food, infection, equipment factor – incl. contaminated, unsafe food or water	High symptom 3.30 Low symptom 2.97 Effect size 0.16, p<0.01
		Ate local food or drank local water, non-mil supplied	High symptom 2.43 Low symptom 2.26 Effect size 0.06, p = 0.06
Gray, 2002 (3,831 Seabee)	GWI	Food poisoning in unit	OR = 2.14 (1.77-2.59) unadj OR = 1.44 (1.13-1.82) sat
		Got food poisoning	OR = 2.53 (1.92-3.34) unadj
		Ate local food	OR = 1.32 (1.13-1.53) unadj
Reid, 2001 (3,531 UK GW vets)	CFS	Local food	OR = 0.8 (0.5-1.4) unadj OR = 0.9 (0.5-1.6) adj
	MCS	Local food	OR = 0.8 (0.4-1.6) unadj OR = 0.9 (0.5-1.7) adj

☆☆ RAC-GWVI

**Epidemiologic Studies: Contaminated Food  
 Associations with Health Outcomes**

Study	Outcome	Exposure	Findings
Kang, 2002		Ate food contaminated w/ smoke, oil, chem	GWV 'cases' 73.4% Non-cases 20.6%
Sudicani, 1999 (667 Danish GW vets)	Neuropsych symptoms: memory, headache, dizziness, fatigue, sleep problems	Ingestion of contaminated food (fumes, oil, chemicals) Ingestion of local food	Bivariate assoc. w/ # symptoms p <= 0.001, n.s. in multivariate model p <= 0.001, n.s. in multivariate model
Unwin, 1999 (2,735 UK GW vets)	CMI	Local food	OR = 1.1 (0.9-1.3)

☆☆ RAC-GWVI

**Epidemiologic Studies: Contaminated Water  
 How Many Were Exposed?**

Study	Population	Exposure		
Kang, 2002	11,441 GW vets	Bathed in or drank water contam. w/ smoke, oil, other chemicals	All vets	28.1%
		Bathed/swam in local pond, river, Gulf	All vets	23.3%
Kroenke, 1998	18,495 CCEP registrants	Non-US water		31.0%
McCauley, 1999	305 GW vets	Water from local taps		34.0%
		Water from local wells		6.0%

☆☆ RAC-GWVI

**Epidemiologic Studies: Contaminated Water  
 How Many Were Exposed?**

Study	Population	Exposure		
Pierce, 2005	495 female GW vets (AF)	Contaminated food or water		Avg. # days exposed 24.75 days
		Bathed/swam in local pond, river, Gulf		6.23 days
Stuart, 2002	54,244 GW vets, CCEP partic.	Contaminated water	Male	11.2%
			Female	11.7%
Vasterling, 2003	72 GW vets, LA NG/reserve	Contaminated shower water		25%
CCEP Report, 1996		Bathed in contaminated water		20%
		Bathed in non-US water		32%
SIU Report		Bathed in contaminated water		28.6%
		Bathed in non-military water		30.5%

☆☆ RAC-GWVI

**Epidemiologic Studies: Contaminated Water  
 Associations with Health Outcomes**

Study	Outcome	Exposure	Findings	
Kang, 2002	11,441 GW vets	Bathed in or drank contaminated water	GWV 'cases'	59.8%
			Non-cases	19.1%
Gray, 2002 (3,831 Seabees)	CMI	Drank contam. water	OR = 3.79 (3.09-4.67) unadj OR = 1.71 (1.32-2.23) sat.	
		Drank water from desert bag	OR = 1.98 (1.66-2.36) unadj OR = 1.38 (1.10-1.72) sat.	
		Bathe in local pond/river/Gulf	OR = 1.76 (1.48-2.09) unadj.	

☆☆ RAC-GWVI

**Epidemiologic Studies: Contaminated Water  
 Associations with Health Outcomes**

Study	Outcome	Exposure	Findings
Haley, 1997 (249 GW vets)	3 syndromes, derived by factor analysis	Drinking water w/ petroleum taste	Impaired Cognition RR = 2.6 (0.9-7.7) Confusion/ataxia OR = 2.8 (1.3-6.3) Arthro-myo-neuropathy OR = 2.6 (1.2-5.6) (All n.s. in multivariate)
Sudanicin, 1999 (667 Danish GW vets)	Neuropsych symptoms: memory, headache, dizziness, fatigue, sleep problems	Bathed in/drank water contam w/ fumes, oil, chemicals  Tooth brushing using water contam w/ chem or pesticides	Bivariate assoc. w/ # symptoms p <= 0.001, OR = 2.9 (1.8-4.6) multivariate model  P <= 0.001, n.s. in multivariate model

☆☆ RAC-GWVI

**Summary:  
Local/Contaminated Food and Water**

---

**Summary: Self/Reported Exposures:**

- Use of local food reported by: ~ 75%  
Use of local water reported by: ~ 30%
- Exposure to contaminated food reported by: ~ 20-30%  
Exposure to contaminated water reported by: ~ 20-30%

☆☆ RAC-GWVI

**Summary:  
Local/Contaminated Food and Water**

---

**Summary: Health Effects**

- Local food: little association with health outcomes  
Local water: *no information*
- Contaminated food: OR~1.5 – 2.5  
Contaminated water: OR ~ 1.8 - 3.8

*Consumption of both contaminated food and water highly associated with GW-factor case status in large VA study*

☆☆ RAC-GWVI

**Summary:  
Contaminated Food and Water**

---

- Widespread exposure to locally-supplied food and water, but little indication of link to poor health
- Epi studies suggest possible associations between chronic symptoms and contaminated food/water
- No data to suggest possible mechanism for such a link; speculative possibilities might include:
  - *Food or water born pathogen associated with chronic "subclinical" infection?*
  - *Acute debilitation caused by food poisoning alters effects of other exposures?*
  - *Toxic effects of ingested oily substances?*
  - *Spurious findings?*

☆☆ RAC-GWVI

**Decontaminating Agents**

---

☆☆ RAC-GWVI

## Decontaminating Agents: DS2

### Decontaminating Solution 2

- Used in the Gulf War to decontaminate equipment exposed to chemical warfare agents
- Principal constituent is 2ME (ethylene glycomonomethyl ether)
  - Widely used in paints, varnishes, industrial solvents
- Animal studies indicate hematological, reproductive effects (testicular damage, diminished fertility)
- Chronic effects after limited exposures? unknown
- One report of soldiers with dermal exposures developed rashes

★★ RAC-GWVI

## CARC Paint

★★ RAC-GWVI

## Chemical Agent Resistant Coating (CARC) Paint

- Thousands of military vehicles and other equipment shipped into theater in association with the Gulf War
- Most of the equipment was still painted green "woodland camouflage" when it arrived
- Urgent need to repaint vehicles to desert camouflage colors
- Painting operations set up to paint large number of incoming vehicles in theater prior to Desert Storm
- After the war, similar operations repainted many vehicles back to woodland camouflage

★★ RAC-GWVI

## Chemical Agent Resistant Coating (CARC) Paint

- A polyurethane paint applied to military equipment
  - > Improve protection from chemical warfare agents
  - > Facilitate decontamination
  - > Extends service life of vehicles and equipment
- CARC contains multiple hazardous compounds (toluene, benzene, crystalline silica, ketone)
- Most concern focused on HDI (hexamethylene diisocyanate) which hardens the paint
- Additional hazardous solvents (paint thinners, cleaners, etc) used in painting operations

★★ RAC-GWVI

### **Chemical Agent Resistant Coating (CARC) Painting Operations**

- First painting operations set up by experienced civilian painting contractors in Sep, 1990 at port of Ad Damman, SA
  - > This group had protective equipment
- Two additional major CARC spray painting operations established by the Army
  - > Ad Damman
  - > Al Jubayl
- These sites operated by a Florida Army National Guard Unit, the 325<sup>th</sup> Maintenance Company
  - > This unit not trained in painting operations, did not have proper protective equipment
- Other, smaller operations also established for shorter periods

☆☆ RAC-GWVI



### **Health effects of CARC exposure**

- Aerosolized, freshly applied paint
  - > Respiratory problems, asthma
  - > Dizziness
  - > Fatigue
  - > Nausea
  - > Headache
  - > Skin rashes
  - > Nausea, vomiting, diarrhea
  - > Sensitization
- After it hardens, CARC (HDI) thought to present a problem only if heated to high temperatures (also if sanded/chipped?)

☆☆ RAC-GWVI



### 325<sup>th</sup> Maintenance Company

- Started painting in Nov 1990; operations lacked proper personal protective equipment, air circulation equipment
- Began reporting health problems during operations (Dec 90 report): dizziness, rashes, vomiting, nausea
- Local command concerned; ANG alerted ARCENT; family members contacted Adj General, Congress
- Onsite investigation of operations at Ad Dammam and Al Jubayl December-June; operations shut down temporarily
- Protective equipment eventually provided

☆☆ RAC-GWVI

### 325<sup>th</sup> Maintenance Company: the Story

- Health, respiratory evaluations provided to all members by Army physician in 1992 during 2-week training period at Ft. Stewart, GA
- Met with representatives of South Florida VBA Regional Office to assist with filing claims
- Regional office handled the issue locally
- What happened?
  - > How many became ill?
  - > What were there symptoms, diagnosed conditions?
  - > Benefits provided?
  - > Effort to assist other units involved in CARC painting operations?

☆☆ RAC-GWVI

### 325<sup>th</sup> Maintenance Company

- No study or data available; no comprehensive report summarizing how many affected and how
- Sources of information
  - > OSAGWI Environmental Exposure Report
  - > 1993 Report to Congress
  - > Information from Florida RO
  - > Information from Congressman Putnam's office
  - > Information from ANG rep, company commander, physician who assisted ill veterans, affected veterans, OSAGWI lead sheets

☆☆ RAC-GWVI

### 325<sup>th</sup> Maintenance Company

- Physician who examined 20-30 veterans in 1992:
  - > Reported paint fumes permeated entire camp:—administrative, eating, sleeping area—at Al Jubayl operations
  - > So much solvent vapor in the air, lights had to be replaced with type that resist explosions
  - > Veterans he examined showed multiple nonspecific symptoms:
    - Headache
    - Fatigue
    - Sleep disturbances
    - Asthma-like symptoms
    - Some became highly sensitized

★★★ RAC-GWVI

### 325<sup>th</sup> Maintenance Company

- Representative of Florida Army National Guard
  - > Problems had been severe in theater: coughed up paint, joint swelling, rashes, respiratory problems, nerve problems
  - > Afterwards, the unit had a lot of problems, not sure if it was Gulf War syndrome or effects of CARC paint
  - > Guard never received funding to do medical evaluations of the whole unit; urged them to go to VA
  - > Many of those in the unit were poor, couldn't get to Tampa VA for evaluation

★★★ RAC-GWVI

### 325<sup>th</sup> Maintenance Company

- Severely ill veteran
  - > Veteran had been a runner, black belt karate instructor
  - > Says lungs are badly damaged from chemicals: wheelchair bound, requires oxygen, "it ate half a lung"
  - > Has lupus, "esophagus closed", allergic to chemicals and perfumes, skin lesions, rash since the war
  - > Described others in unit who had brain and/or lung cancer, says about 8 had died so far
  - > He is 100% service connected; took 5 years

★★★ RAC-GWVI

### 325<sup>th</sup> Maintenance Company

- VA Regional Office in St. Petersburg, FL
  - > Handled the issue locally, established guidelines for service connection
  - > All members of the unit presumed exposed to CARC; veterans filed claims, required opinion of doc performing C&P exam
  - > CARC-specific service connection allowed only for respiratory and skin problems; other symptoms/undiagnosed conditions not S-C
  - > Tried very hard to service-connect "applied any and all laws"
  - > Some claims still pending: Recalled about 200 cases processed, but CARC cases not specifically collated. +As of June, 1993:
    - 70 individuals from 325<sup>th</sup> listed in VA files
    - 20 had filed claims: 6 pending, 8 denied, 6 service connected
    - Claims involving resp/env hazard: 2 s/c, 4 denied

★★★ RAC-GWVI

### 325<sup>th</sup> Maintenance Company

- Dr. Bruce Pettyjohn
  - > Was medical officer for the 325th; did exams predeployment and postdeployment
  - > Most patients had memory problems, skin rashes, muscle pain, GI problems; not sure how much was due to CARC, other exposures
  - > Wrote ~ 50 page report for about 200 veterans to assist with benefits applications
  - > VA “poo-pooed” the problem
  - > Some have died from various causes; he thinks they deserve purple hearts

### Epidemiologic Studies: CARC Paint How Many Were Exposed?

Study	Population	Exposure		
Kang, 2000	11,441 GW vets	CARC paint	All veterans	21.7%
			VA registry vets	35.0%
Kroenke, 1996	18,495 CCEP registrants	CARC paint		48.0%
Stuart, 2002	54,244 GW Vets, CCEP partic.	CARC paint	Male	31.1%
			Female	20.3%
Australian GW Study	1,456 Austr. GW vets	contact with wet CARC paint		1.3%

### Epidemiologic Studies: CARC Paint Association with Health Outcomes

Study	Outcome	Exposure	Findings
Haley, 1997 (249 GW vets)	3 syndromes, derived by factor analysis	Near enough to smell CARC paint sprayed	Impaired Cognition RR = 0.9 (0.1-6.9) Confusion/ataxia RR = 3.2 (1.3-8.0) Arthro-myo-neuropathy RR = 1.6 (0.5-5.1)
Spencer, 2001 (1,119 GW vets)	CHL	Painted with CARC	OR = 3.29 (1.88-5.76)
Kang, 2002	11,441 GW vets	CARC paint	GW 'cases' 51.2% Non-cases 16.3%

### CARC Paint: Epidemiologic Findings

- ~20 % Gulf veterans report exposure to CARC paint; higher among Registry participants
- Association of s/r CARC paint exposure to multisymptom complexes: OR ~ 3.0

### CARC Paint: Summary

---

- Appears that excess exposure to CARC paint did occur in some individuals, likely resulted in serious health problems
- Epi studies suggest possible association with multisymptom illness
- Most information available on the 325<sup>th</sup> Maintenance Co.
- No reports identified that summarized clinical findings in this group, or other CARC-exposed groups
- Unclear whether symptoms of these veterans all due to CARC, or potentially related to other causes
- Little info re: effects of CARC exposures with other painting operations

### Misc exposures

---

### Additional Exposures Potentially Associated with Adverse Health Effects

---

#### Misc

- > Hydraulic fluid
- > Purple T shirt incident
- > Other industrial exposures?

### Exposure to Hydraulic Fluid

Study	Outcome	Exposure	Findings
Spencer, 2001 (1,119 ORN/A GW vets)	CMI	Cleaned hydraulic leaks	OR = 2.45 (1.31-4.58) unadjusted

## Presentation 11 – Susan Proctor

### **SPATIAL ANALYSIS OF 1991 GULF WAR TROOP LOCATIONS IN RELATIONSHIP WITH POSTWAR HEALTH SYMPTOM REPORTS USING GIS TECHNIQUES**

Susan P. Proctor, DSc; Sucharita Gopal, PhD;  
Asuka Imai, MA; Jessica Wolfe, PhD, MPH;  
David Ozonoff, MD; Roberta F. White, PhD

Boston Environmental Hazards Center; Boston University Schools of Public Health and Medicine; National Center for PTSD; Boston University Department of Geography

Presented at Meeting of the  
Research Advisory Committee on Gulf War Veterans' Illnesses  
September 20, 2005

### **PRESENTATION OUTLINE**

- Overview of GIS
- Application of GIS to study of GW veterans' health
- Research study
- Discussion
- Other research projects

### **OVERVIEW OF GIS**

GIS= Geographic Information Systems

GIS technology is a database tool that enables the

- Input
  - Storage
  - Management
  - Analysis
  - Display
- } of both geographic & non-geographic data into a database structure

### **GIS IN PUBLIC HEALTH**

GIS, combined with temporal-spatial analysis methods,

-provide a methodology for understanding associations between location, environment, and disease.

#### **Application Examples**

- Hookworm infection/reinfection in S. Africa (Saathoff et al., 2005)
- Arsenic in drinking water in Bangladesh (Hassan et al., 2003)
- Herbicide exposures in Vietnam (Stellman et al, 2003)

### KNOWLEDGE GAPS IN STUDY OF 1991 GULF WAR VETERANS' HEALTH CONCERNS

---

- Lack of baseline, pre-deployment health and lifestyle information to be able to examine influence on post-deployment health outcomes.
- Health outcomes often measured long after deployment.
- No uniform description of health outcomes consistent across GW veterans.
- Over-reliance on self-report measures of outcome and exposure variables.
- Lack of objective environmental exposure data to examine exposure-health effect relationships.

### APPROACHES USED WITH SURROGATE EXPOSURE MEASURES

---

- ✓ Time period of deployment (Spencer et al., 1998)
- ✓ Reported movement into different regions (Steele et al., 2000)
- ✓ Unit-level troop locations coupled with modeled exposure estimates, to oil fire smoke (Lange et al., 2002) and Khamisiyah plume (McCauley et al., 2002; Smith et al., 2003)
- ✓ Spatial analyses of troop locations to examine patterns (this study)

### RESEARCH OBJECTIVE

Examine whether the GW locations of soldiers who are categorized as having severe postwar chronic multisymptom illness display local and global spatial autocorrelation patterns.

---

Were troops, who later became ill, clustered in particular locations at the points of time of interest during their deployment?

→ If so, further investigation into unique exposure scenarios present at these locations at these timepoints can help frame hypotheses for further study.

### DEVENS COHORT STUDY BACKGROUND

---

DEVENS Cohort: Prospective study of US Army Active, Reserve, and National Guard GW veterans.

Time 1: Survey, Spring 1991 (n = 2,949)

Time 2: Survey, Winter 1992/Spring 1993  
(n = 2,313)

Time 3: In-person assessments, Fall 1994/  
Summer 1996; Stratified, random sample  
of larger cohort (n=220)

Time 4: Survey, Fall 1997/Fall 1998 (n=1,291)

### CHARACTERISTICS OF DEVENS COHORT AT TIME 1 (n=2,949)

	Mean (SD)/ Percent	Range
Age (years)	30.2 (8.4)	19-65
Education (years)	13.2 (1.8)	7-24
Gender (% female)	8.1	
Race:		
% white	82.8	
% black	8.7	
Service type:		
% Guard	51.6	
% Reserve	20.2	
% Active	28.2	

### PUBLISHED REPORTS TO DATE FROM THE DEVENS COHORT STUDY

- ✦ Traumatic events/exposures and PTSD symptomatology
- ✦ Sexual harassment and PTSD symptomatology
- ✦ GW environmental exposures and health symptomatology
- ✦ GW environmental exposures and cognitive functioning
- ✦ Troop locations during the GW and health symptomatology
- ✦ Relationship of psychiatric status to GW veterans' health
- ✦ Rates of MCS, CFS, and CMI
- ✦ Health-related quality of life (SF36)
- ✦ Changes in PTSD over time

### DEVENS COHORT STUDY BACKGROUND

**DEVENS Cohort:** Prospective study of US Army Active, Reserve, and National Guard GW veterans.

- Time 1: Survey, Spring 1991 (n = 2,949)
- Time 2: Survey, Winter 1992/Spring 1993 (n = 2,313)
- Time 3: In-person assessments, Fall 1994/ Summer 1996; Stratified, random sample of larger cohort (n=220)
- Time 4: Survey, Fall 1997/Fall 1998 (n=1,291)

### ENVIRONMENTAL-GEOLOCATION INTERVIEW STRUCTURE

- Deployment descriptive information: dates, units, & job types
- Deployment location information (with assessment of recall ability)

### GROUP DEMOGRAPHICS AND DEPLOYMENT CHARACTERISTICS

Study Group (n=173)	
Age	34.5 (9.4) [range: 22-61]
Education	13.9 (2.2) [range: 9-24]
% Female	47%
% Reserves/NG	89%
# weeks deployed	18.7 (6.2) [range: 5-36]
% moved > 3 times	82%
% unit moved together	65%
% went into Kuwait	39%
% went into Iraq	44%

DATE PERIODS EXAMINED	MARKER DEPLOYMENT EVENTS
-----------------------	--------------------------

#1 Second week in December 1990	Pre-combat phase
#2 Third week in January 1991	Air offensive begins; first Scud missile launched against US and allies
#3 Second week in February 1991	Oil wells were set on fire by retreating Iraqis in late January/early February, 1991
#4 Fourth week in February 1991	Allied ground war began 24 Feb 1991 and ended with the cease-fire 28 Feb 1991
#5 First week in March 1991	The demolition of munitions at Khamisiyah pit and demolition of bunker at Khamisiyah, Iraq
#6 Second week in April 1991	Post-combat phase

### CHRONIC MULTISYMP TOM ILLNESS CASE CRITERIA

- Two or more of the following three self-reported symptoms :
  - fatigue**
  - mood-cognition** (feeling depressed, difficulty remembering or concentrating, feeling moody, feeling anxious, trouble finding words, or difficulty sleeping)
  - musculoskeletal** (joint pain, joint stiffness, or muscle pain)
- Chronic presence (six months or longer)

### CHRONIC MULTISYMP TOM ILLNESS CATEGORIZATION

CMI	Study Group (n=173)
None	31%
Mild-to-moderate	34%
Severe	35%

### SPECIFIC RESEARCH QUESTIONS

Examining each time period separately:

**Question #1:** Are there significant clusters of cases (persons with post-war severe CMI) when looking globally over the entire geographical region?

**Question #2:** Are there significant pockets or clusters of cases at specific identified locations, when compared to neighboring areas?

### RESEARCH QUESTION #1

Examining each time period separately:

**Are there significant location clusters of cases (persons with post-war severe CMI) when looking globally over the entire geographical region?**

**USE: Global Moran's I statistic**

### Global Moran's I – Hypothesis

**Global Moran's I Statistic** to examine spatial patterns over region

**H<sub>0</sub>:** The spatial distribution of the veterans, who postwar met criteria for severe CMI, is random.

**H<sub>1</sub>:** The spatial distribution of the veterans, who postwar met criteria for severe CMI, is not random; there is a significant spatial pattern.

### Global Moran's I – Results

Date Period	Group meeting severe postwar CMI criteria (maximum n=60)		Group not meeting severe postwar CMI criteria (maximum n = 113)		Overall Study Group (maximum n = 173)	
	I	Z(I)	I	Z(I)	I	Z(I)
2 <sup>nd</sup> _Dec_90	0.268	3.815 *	-0.012	0.016	0.118	1.787
3 <sup>rd</sup> _Jan_91	0.093	1.441	-0.073	-0.817	0.06	0.996
2 <sup>nd</sup> _Feb_91	0.016	0.396	-0.06	-0.632	-0.016	-0.03
4 <sup>th</sup> _Feb_91	-0.041	-0.381	0.046	0.805	-0.011	0.031
1 <sup>st</sup> _March_91	0.1	1.537	-0.066	-0.711	-0.009	0.055
2 <sup>nd</sup> _April_91	-0.024	-0.145	-0.09	-1.047	0.029	0.571

\* p < 0.05

## RESEARCH QUESTION #2

Examining each time period separately:

**Question #2: Are there significant pockets or clusters of cases at identified locations, when compared to neighboring values?**

**USE: Local G\* statistic**  
 (compared to outside buffer area)

**USE: Local Moran's I statistic**  
 (compared to within buffer area)

## LOCAL STATISTICS-HYPOTHESIS

Examination of spatial patterns of cases within location regions, determined by buffer area dimensions

H<sub>0</sub>: The spatial distribution of the veterans meeting criteria for severe CMI is random, when comparing between neighboring locations and defined by buffer differences.

H<sub>1</sub>: The spatial distribution of the veterans meeting criteria for severe CMI is not random and there is a significant spatial pattern/clustering, when comparing between neighboring locations and defined by buffer differences.

## SUMMARY OF RESULTS FROM LOCAL STATISTICS

### Local G\* statistics- significant local clusterings observed\*

Dhahran/Dammam area → second week Dec 1990  
 → third week Jan 1991

KKMC/Log Base Echo area → third week Jan 1991  
 → second week Feb 1991

An Nasiriyah area of Iraq → first week March 1991

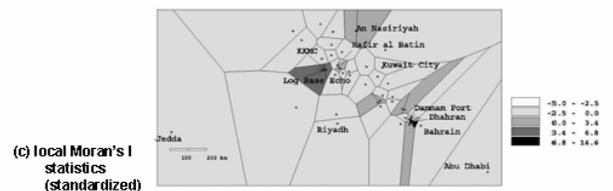
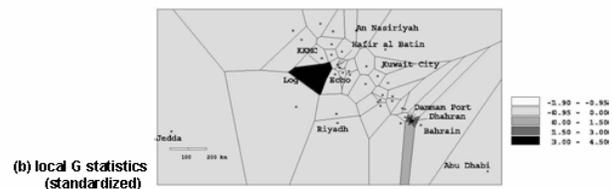
### Local Moran's I statistics- significant local clusterings observed \*

Dhahran/Dammam area → second week Dec 1990  
 → third week Jan 1991

KKMC/Log Base Echo area → third week Jan 1991

\* Bonferroni correction applied

## CMI Rates: 3<sup>rd</sup> week in January, 1991



### Flow of Troop Locations Over Time

Question- Are the hotspots simply artifacts of troop deployment patterns, as they appear to follow general flow of troops during the 1991 Gulf War?

Additional analyses to examine whether hotspots could be explained primarily by troop flow

1. Examined whether the same persons were included in the significant location clusters over time.

**Result:** Clusters did not always contain the same individuals across time

2. G statistics calculated for group not meeting criteria for severe CMI and examined spatial pattern over same date periods

**Result:** Two previously identified significant hotspots (Dhahran/Dammam area in 2<sup>nd</sup> week in Dec 1990 & KKMC/Log Base Echo area in 2<sup>nd</sup> week in Feb 1991) were present both for veterans reporting severe CMI and those who did not meet the criteria for severe CMI

### SUMMARY OF RESULTS FROM LOCAL STATISTICS- CONCLUSIONS\*\*

#### Significant local clusterings observed

Dhahran/Dammam area → third week Jan 1991

KKMC/Log Base Echo area → third week Jan 1991

\*\* After taking into consideration Bonferroni correction for multiple comparisons, flow pattern of troop movements, and results from both local  $G^2$  and Moran's  $I$  statistics.

### DISCUSSION ITEMS

- ✓ Use of interview data (rationale)
- ✓ Comparison of severe cases vs. others (rationale)
- ✓ Bonferroni factor-multiple comparison adjustments
- ✓ Issues of flow of troop movements
- ✓ GIS limitations & integration with statistics

### POTENTIAL NEXT STEPS

- Confirm findings with larger and diverse cohort.
- Apply methodology to examine other health outcomes.
- Explore the potential applicability of complex spatio-temporal GIS and statistical techniques to research questions.
- Identify exposure-effect hypotheses to target in further epidemiologic research.
- Identify lessons learned from the research challenges in investigations of 1991 GW veterans' health to improve future force health protection.

**CURRENT ONGOING  
RESEARCH**

### Presentation 12 – Mihaela Aslan

#### ACETYLCHOLINESTERASE ACTIVITY IN GULF WAR DEPLOYED AND ERA VETERANS: SEP '05 UPDATE

Mihaela Aslan, Ph.D. (West Haven)  
John Concato, M.D., M.S., M.P.H. (West Haven)  
Bradley Doebbeling, M.D., M.Sc. (Indianapolis)  
Margaret Palmisano, Ph.D. (West Haven)  
Peter Peduzzi, Ph.D. (West Haven)  
Hermona Soreq, Ph.D. (Jerusalem)

#### OVERVIEW OF PROJECT

- Original questionnaire study conducted among deployed and non-deployed veterans in Iowa Gulf War Cohort Study (B. Doebbeling, et al.)
- Potential role of cholinergic enzyme activity proposed (e.g., neurologic processes may have been affected by deployment to Persian Gulf, H. Soreq, et al.)
- VA project was organized; original analyses completed; **additional analyses of AChE-R presented today**

#### DETAILS RE: SOURCES OF DATA

##### Questionnaire responses from Iowa Gulf War Cohort Study

- Wave I: 3,695 veterans of Persian Gulf era, from Iowa
- Wave II: 374 case patients with cognitive dysfunction, depression, or chronic widespread pain; 228 controls without these conditions (N=602 subset of Wave I)

##### Laboratory assays (of stored sera) at Hebrew University

- Acetylcholinesterase (AChE)
- Butyrylcholinesterase (BChE)
- Paraoxonase, Arylesterase (PON1, Aryl)
- **R splice variant of Acetylcholinesterase (AChE-R)**

#### DETAILS RE: METHODS

- Questionnaire data transferred, data dictionaries reviewed, study variables defined and coded
- Blood samples shipped; original laboratory assays conducted; **AChE-R measured in second phase of project**
- Data from questionnaires and laboratory assays merged
- Analyses of original hypotheses completed; **analyses of AChE-R presented today**

#### OVERVIEW OF ORIGINAL ANALYSES

- Framework for research questions: Are pertinent factors associated with enzyme levels?
- Factors studied:
  - standardized testing for anxiety/mood disorders
  - deployment status re: service in Persian Gulf
  - Gulf War Veterans Illness (GWVI)

#### FORMAT OF ORIGINAL ANALYSES

- Multiple linear regression analyses conducted with enzyme levels assigned as outcome variables; results presented as predicted least square mean values (nmol/min/ml)
- Models adjusted for age, body-mass index, smoking, acute illness, antidepressant medications, alcohol/drug use, case-control status in Iowa study

#### FINAL STUDY SAMPLE FOR ORIGINAL ANALYSES

<u>Wave II participants:</u>	<u>602</u>
• serum not available	- 25
<u>Study population:</u>	<u>577</u>
• non-white or female veterans	- 89
• incomplete questionnaire data	- 12
<u>Final analytic sample:</u>	<u>476</u>

#### SUMMARY OF ORIGINAL ANALYSES

- Anxiety/mood disorders not associated with enzyme levels
- Deployment status not associated with enzyme levels
- GWVI symptoms not associated with enzyme levels

#### OVERVIEW OF CURRENT ANALYSES

- Framework for research questions: Are pertinent factors associated with AChE-R levels?
- Factors studied:
  - standardized testing for anxiety/mood disorders
  - deployment status re: service in Persian Gulf
  - Gulf War Veterans Illness (GWVI)
  - self-reported exposures among deployed veterans

#### GULF WAR VETERANS ILLNESS

Pertinent symptoms reported at Wave I or II were linked to CDC criteria for GWVI (e.g., involving 2 of 3 axes re: mood-cognitive, fatigue, musculoskeletal symptoms)

GWVI: Definition 1 - onset of symptoms after Gulf War, present at Wave II, regardless of status at Wave I;  
Definition 2 - onset after Gulf War, present at Wave I and Wave II (subset with longer duration of symptoms)

#### FORMAT OF CURRENT ANALYSES

- Multiple linear regression analyses conducted with AChE-R levels assigned as outcome variables; results presented as predicted least square mean values (normalized Kamovski arbitrary units)
- Models adjusted for age, body-mass index, smoking, acute illness, antidepressant medications, alcohol/drug use, case-control status in Iowa study

#### FINAL STUDY SAMPLE FOR CURRENT ANALYSES

<u>Original study population:</u>	<u>577</u>
• serum not available	- 321
<u>Current study population:</u>	<u>256</u>
• non-white or female veterans	- 38
• incomplete questionnaire data	- 4
<u>Final analytic sample:</u>	<u>214</u>

VETERANS WITH AND WITHOUT AChE-R ASSAYS

<u>Characteristic:</u>	<u>AChE-R available:</u>	
	<u>Yes (N=256)</u>	<u>No (N=321)</u>
	<u>%</u>	<u>%</u>
• male sex	88%	87%
• mean age	(39 years)	(39 years)
• mean body mass index	(29)	(29)
• deployed	73%	71%
• GWVI definition 1	66%	61%
• GWVI definition 2	36%	32%

RESULTS OF LABORATORY ASSAYS

Measurement of AChE-R for 256 veterans:

Range	0-106
Median	39
Mean	42
Standard deviation	±21

*[OTHER TABLES BEING CHECKED*

*PRIOR TO PUBLICATION]*

SUMMARY OF CURRENT ANALYSES

- Deployment to Persian Gulf not associated with AChE-R
- Symptoms of Gulf War Veterans Illness not associated with AChE-R
- Data regarding self-reported exposure and AChE-R limited (e.g., alpha-level not adjusted for multiple comparisons; very low frequency of non-exposed is “unstable” result)

**Presentation 13 – Tim Bullman**



**Mortality in US Army Gulf War  
Veterans Possibly Exposed to 1991  
Khamisiyah Chemical Munitions  
Destruction**

Tim A. Bullman, M.A.  
Clare M. Mahan, Ph.D.  
Han K. Kang, Dr.P.H.  
William F. Page, Ph.D.



**Background**

- Army-sponsored study of 351,000 deployed Army personnel.
- Risk factor was possible chemical warfare agent exposure.
- Investigate independently the effects of notification of possible exposure.

2



**Background**

- Individual exposure estimates were made using information from nerve agent dispersion and meteorologic models along with troop location data.
- The latest exposure estimates (2000 DoD model) are being used in our analyses.

3



**Methods**

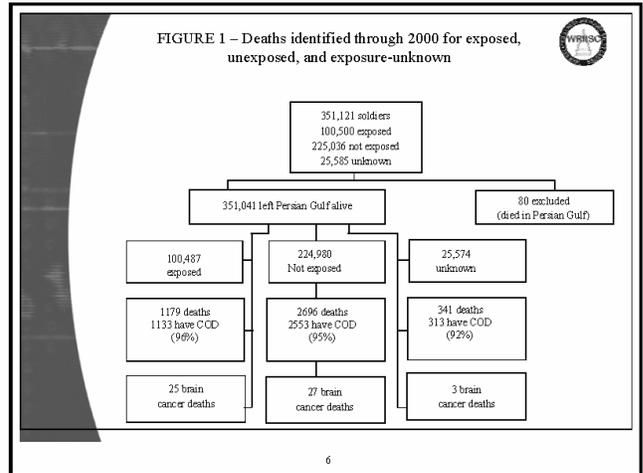
- 351,041 deployed Army veterans using data from DoD deployment health files.
  - Divided into 3 groups:
    - exposed (100,487),
    - unexposed (224,980),
    - exposure status unknown (25,574).

4

### Methods

- **Vital status** was determined using VA and SSA records.
- **Cause of death** through December 31, 2000 came from National Death Index.
- For brain cancer deaths,
  - Hard copy death certificates and relevant medical records were obtained for additional review.

5



### Methods

- **Demographic data** from Defense Manpower Data Center:
  - age, race, gender, rank, unit component, military occupational specialty, etc.
- **Further data** on the number of days in the hazard area (0, 1, 2, 3, 4) came from DoD Deployment Health.
- Smoke exposure data came from Army (CHPPM)

7

### Methods

- **Crude death rates**
- **Unadjusted relative risk estimates**
- **Adjusted relative risk estimates derived from Cox Proportional Hazard Model.**

8

## Methods

- **Covariates included**
  - Age,
  - Race (white, non-white),
  - Gender,
  - Rank (enlisted, officer, warrant officer),
  - Unit component (active duty, National Guard, reserves).

9

## RESULTS

**TABLE 1 – Khamisiyah, Iraq, 1991 Chemical Munitions Destruction Exposure Status for US Army Gulf War Veterans, by Selected Demographic and Service Characteristics**

	All Exposed (n=100467)		All Unexposed (n=224980)		Exposure Unknown (n=25574)	
	#	%	#	%	#	%
Age in 1990						
≤ 21	23421	(23.3)	56509	(25.1)	4951	(19.4)
22-25	25825	(25.7)	58352	(26.2)	6795	(26.6)
26-31	24364	(24.2)	54982	(24.4)	6302	(24.6)
≥ 32	26877	(26.8)	54637	(24.3)	7526	(29.4)
Mean age in 1990 y	27.7		27.2		28.2	
Race						
White	65146	(64.8)	145009	(64.5)	16849	(65.9)
Non-White	35341	(35.2)	79971	(35.5)	8725	(34.1)
Gender						
Male	89777	(89.3)	204594	(90.9)	22225	(86.9)
Female	10710	(10.6)	20386	(9.1)	3349	(13.1)
Rank						
Enlisted	88802	(88.4)	202093	(89.8)	22161	(86.7)
Warrant Officer	1862	(1.8)	4728	(2.1)	703	(2.7)
Officer	9823	(9.8)	18159	(8.1)	2710	(10.6)
Unit Component						
Active	76464	(74.1)	175089	(77.8)	17745	(69.4)
Guard	11897	(11.8)	24445	(10.9)	1011	(3.9)
Reserve	14126	(14.1)	25446	(11.3)	6818	(26.7)

10

## RESULTS

# of days exposed	# Days Exposed	
	#	%
1	86167	85.7
2	12551	12.5
3	1657	1.7
4	112	0.1

11

## RESULTS

**TABLE 2 – Cause-Specific Mortality Among Exposed US Army Gulf War Veterans at Khamisiyah, Iraq, in 1991 Compared With Unexposed Army Veterans**

Underlying cause of death (ICD-9)	Exposed (n=100467) No. (Rate)	Not Exposed (n=224980) No. (Rate)	Relative Risks		
			Crude	Adjusted	95%CI
All causes	1179 (12.22)	2696 (12.47)	0.98	0.97	0.91, 1.04
All diseases (001-799)	496 (5.14)	1093 (5.05)	1.02	0.96	0.86, 1.07
Infectious and parasitic disease (001-139)	29 (0.30)	56 (0.26)	1.16	1.16	0.74, 1.82
Malignant neoplasm (140-208)	184 (1.91)	391 (1.81)	1.06	0.97	0.82, 1.16
Colon cancer (153)	14 (0.15)	26 (0.12)	1.25	1.17	0.61, 2.25
Lung cancer (162)	30 (0.31)	84 (0.39)	0.80	0.72	0.47, 1.10
<b>Brain cancer (191-192)</b>	<b>25 (0.26)</b>	<b>27 (0.12)</b>	<b>2.17</b>	<b>1.94</b>	<b>1.12, 3.34</b>
Disease of circulatory system (390-459)	170 (1.76)	407 (1.88)	0.94	0.89	0.74, 1.06
Disease of respiratory system (460-519)	22 (0.23)	45 (0.21)	1.10	1.03	0.62, 1.72
Disease of the digestive system (520-579)	24 (0.25)	46 (0.21)	1.17	1.10	0.67, 1.81
All external causes (E800-E989)	637 (6.60)	1460 (6.75)	0.98	1.01	0.92, 1.10

12

**RESULTS**

**TABLE 2 – Cause-Specific Mortality Risk Among US Army Gulf War Veterans Exposed at Khamsiyah, Iraq, in 1991 Compared With Unexposed Army Gulf War Veterans**

Underlying cause of death (ICD-9)	1 Day Exposure	≥ 2 Day Exposure	All Nonexposed	1-Day	≥ 2-Day
	(n=86167)	(n=14320)	(n=224980)	Exposure	Exposure
	No. (Rate)	No. (Rate)	No. (Rate)	RR (95%CI)	RR (95%CI)
All causes	1020 (12.34)	159 (11.51)	2696 (12.47)	0.97 (0.90, 1.04)	0.96 (0.82, 1.13)
All diseases (001-799)	427 (5.17)	69 (5.00)	1093 (5.05)	0.95 (0.83, 1.06)	1.06 (0.83, 1.30)
Infectious and parasitic diseases (001-139)	24 (0.29)	5 (0.36)	56 (0.26)	1.11 (0.69, 1.80)	1.49 (0.59, 3.74)
Malignant neoplasms (140-208)	156 (1.89)	28 (2.03)	391 (1.81)	0.94 (0.78, 1.13)	1.25 (0.85, 1.84)
<b>Brain cancer (191-192)</b>	<b>19 (0.23)</b>	<b>6 (0.43)</b>	<b>27 (0.12)</b>	<b>1.72 (0.95, 3.10)</b>	<b>3.26 (1.33, 7.96)</b>

13

**RESULTS**

**Brain Cancer Deaths by Length of Exposure**

# Days Exposed	# Deaths	Rate/100,000 Persons
0 Days	27	11.97
1 Day	19	22.05
2 Days	5	39.83
3 Days	1	60.35
4 Days	0	0.00

14

**RESULTS**

**Distribution Of Primary Cancer Cell<sup>1</sup> Type By Exposure Status For Brain Cancer Deaths**

Cell Type <sup>2</sup>	Exposure Status		
	Exposed (n=20)	Unexposed (n=21)	Unknown (n=2)
Astrocytoma	4	5	1
Glioblastoma	13	12	1
Glioma <sup>2</sup>	2	2	
Oligodendroglioma	1	2	

<sup>1</sup>Pathological classification for the balance of four confirmed primary tumors are not available. Richard Johnson, MD, Johns Hopkins University, who was blinded to exposure status, reviewed all available records to determine the type of primary brain cancer.

<sup>2</sup>Is a larger grouping of specific cell types

(An additional 3 were classified as primary brain tumors, but cell type not provided)

15

**Results**

**Exposure risk assessment using verified primary brain cancers**

- Analysis of risk using only 44 confirmed primary brain cancer
- Exposed RR, 1.88 (1.04-3.41)
- Exposed 1 Day: RR=1.66
- Exposed 2 Days: RR=3.25

16



## Results

### Risk of Brain cancer death by latency

- 1) Beginning of follow-up-1/31/94 (3 years) 6 exposed/7 unexposed. RR; 1.80, 95% C.I., 0.60-5.36.
- 2) 2/1/94-7/31/97. (6 years) 5 exposed/10 unexposed. RR; 0.99, 95% C.I., 0.34-2.91.
- 3) 8/1/97-12/31/00. (9 years) 14 exposed/10 unexposed. RR; 3.03, 95% C.I., 1.34-6.82

17



## Results

- For **exposure misclassification** to have affected the results, a minimum of three brain cancer deaths among the exposed would have to be reclassified as unexposed.
- Assigning all of veterans with **unknown exposure status** to either the exposed group or the unexposed group did not affect the results.

18



## Results

- **Modeled Oil Well Fire Smoke Data**
  - # days modeled exposure x average concentration of TSP
  - # days at TSP level of 0.260 mg/m<sup>3</sup> or more x average concentration of TSP level for those days
  - the presence or absence of TSP exposure of 0.260 mg/m<sup>3</sup> or greater
- Including each smoke exposure variable into model along with Khamisiyah exposure, did not diminish risk of brain cancer death associated with Khamisiyah exposure.

19



## Discussion

- Only brain cancer mortality was significantly associated with possible chemical warfare agent exposure.
- There was a gradient of risk with number of days of possible exposure.
- Risk of brain cancer death increased as length of follow-up increased.

(Neither exposure misclassification nor missing exposure data could have easily accounted for this finding.)

20



### Discussion

- Limiting deaths to verified primary brain cancers did not affect the finding.
- Adding smoke exposure (total suspended particulate) as a covariate did not affect the results.

21



### Discussion

- We did not have accurate, individual exposure measurements, but exposure status based on plume modeling and unit location.
- Possible sarin exposure may actually be a proxy for some other, causative exposure.
- Multiple hypothesis testing may have lead to a spurious statistically significant association.

22



### Discussion

- Biological Plausibility
  - Neither sarin nor cyclosarin exposure have previously been linked to brain cancer.
- Latency Period
  - The 1-10 year latency period reported in this study is shorter than that reported elsewhere.

23



### Ideas for Future Work

- Do another mortality follow-up when sufficient time has passed.
- Look at brain cancer and other mortality in non-Army military personnel, presumably largely unexposed.
- Plot geographic location of brain cancer deaths.
- Consider update/review of exposure model.
- Consider studies of other risk factors.

24

**Presentation 14 – Paul Levine**

**Cancer Patterns in Gulf and Non-Gulf Veterans**

The George Washington  
University School of  
Public Health and Health  
Services

Paul H. Levine, M.D.  
Heather A. Young, Ph.D.  
Samuel Simmens, Ph.D.

Environmental  
Epidemiology Service  
Dept. of Veterans Affairs

Han K. Kang, Dr.P.H.  
Clare M. Mahan, Ph.D

*Preliminary analytic results in this slide  
presentation are provided for update purposes  
only.*

*Because these analyses are preliminary in nature ,  
they are subject to change following additional data  
analyses.*

**Background**

- 1995–AIDS-Cancer Matching Program successfully uses an Automatch program to match files from AIDS and Cancer registries to document previously undetected cancers associated with AIDS while preserving patient confidentiality... Cote et al. Prev. Med. 1995; 24 : 375-7.
- 1996–Presidential Advisory Committee on Gulf War Veterans' Illnesses recommends long-term studies to investigate cancer rates.
- The North American Association of Central Cancer Registries begins to establish standard procedures for cancer registration in all 50 states and the District of Columbia

**Methods**

- Files obtained from the Defense Manpower Data Center provided a file with 621,902 veterans arriving in the Persian Gulf between 8/2/90 and 3/1/91 and 746,248 non-Gulf veteran controls.
- Database included names, demographic data, and military service information.

### Pilot Study

- Automatch used by New Jersey, a participant in the AIDS-Cancer Matching Program, to match records of New Jersey cancer cases 1991-1999. 135 matches.
- SAS used for match with DC and 323 matches for the years 1991-1999.
- Testicular cancer significantly associated with deployment to the Persian Gulf. Increase apparent 2-3 years after deployment and peaked 4-5 years later.
- Brain cancer and non-Hodgkin's Lymphoma had a suggestive association

Levine et al. Military Medicine 2005;170(2):149-153

### Follow-up Study

- Three year project supported by ASPH/CDC allowed matching with 6 additional states: California, Florida, Maryland, New York, Illinois, and Texas providing additional matches, 2054 in Gulf and 3383 in non-Gulf veterans.

### Demographics

- ~70% of both groups were white and 18% were black
- 86% of the Gulf deployed were males and 79% of the non-Gulf deployed were males
- ~50% of both groups were Army
- Average age in 1991 +/- SD
  - Gulf: 34.3 +/-9.8
  - Non-Gulf: 38.2 +/-10.3
- Average age at diagnosis +/- SD
  - Gulf: 40.6 +/-10.5
  - Non-Gulf: 44.32 +/-10.9
- Active Duty Status
  - Gulf: 80 % Active; 14% Reserve; 6% Guard
  - Non-Gulf: 68% Active; 24% Reserve; 9% Guard

### Results by State

State	Population (millions)	Veteran Population (millions)	# of matches		Crude* PIR (95% CI)		
			Gulf	Non-Gulf	Testicular	Brain	NHL
California	33.9	2.6	481	769	1.2 (0.97-1.5)	1.3 (0.93-1.8)	0.8 (0.6-1.2)
Texas	20.9	1.8	637	965	1.3 (1.1-1.6)	1.1 (0.9-1.5)	1.1 (0.9-1.4)
New York	18.9	1.4	213	425	0.9 (0.6-1.4)	1.3 (0.6-2.7)	1.4 (0.7-3.1)
Florida	15.9	1.9	485	839	0.9 (0.6-1.4)	2.0 (1.1-3.6)	1.3 (0.8-2.1)
Illinois	12.4	1.0	184	304	0.8 (0.5-1.3)	0.9 (0.5-1.7)	1.0 (0.6-1.8)
New Jersey	8.4	0.7	45	91	1.7 (0.4-4.4)	1.0 (0.2-5.4)	0.4 (0.1-1.6)
Maryland	5.3	0.5	54	81	0.99 (0.3-3.9)	0.9 (0.4-2.3)	0.6 (0.2-2.1)
DC	0.6	0.04	108	203	3.8 (1.3-8.6)	1.5 (0.3-4.1)	1.8 (0.7-4.2)

### Combined Results

- 2167 matches in Gulf and 3560 matches in non-Gulf\*
- Crude PIRs (95% CI)
  - Testicular Cancer: 1.22 (1.01-1.47)
  - Brain Cancer: 1.38 (1.08-1.77)
  - NHL: 1.10 (0.80-1.38)
- **Adjusted PIRs (95% CI)**
  - **Testicular Cancer: 0.9 (0.7-1.1)\*\***
  - **Brain Cancer: 1.1 (0.8-1.5)\*\*\***
  - **NHL: 0.9 (0.7-1.1)\*\*\***

\*Only those with diagnosis after 1991 and overlap with DC and MD removed.  
\*\* Adjusted for age, age<sup>2</sup>, and race  
\*\*\*Adjusted for age, age<sup>2</sup>, and race

### Conclusions to Date

- Matching of cancer records with deployment status is feasible and eventually can be performed on a nationwide basis.
- Within particular states, results are suggestive for testicular and brain cancer but thus far no significant differences in combined data.
- Analysis and addition of states are continuing. Interstate differences need to be investigated.

### Future Plans (1)

- 1) Additional matches  
Pennsylvania, Ohio, Michigan, Georgia, North Carolina, Massachusetts, Indiana, Washington, Missouri, Wisconsin, Arizona  
Population=84.2 million  
Estimated Civilian Veteran Population=8.3 million  
Est. cases/year=351,000  
(States chosen in order of population, all NAACCR gold or silver certification)

### Future Plans (2)

2. Investigate reasons for state differences
  - Deployment site of reservists
  - Background cancer patterns
  - Registry methodology
3. Consider another match in 5-10 years to allow for longer latent periods

### Key Studies

- Gray GC, Coate BD, Anderson CM, Kang HK et al. The Postwar Hospitalization Experience of U.S. Veterans of the Persian Gulf War *N Engl J Med.* 1996; 335: 1505-1513.
- Garland FC, Gorham ED, Garland CF et al. Testicular cancer in U.S. Navy Personnel. *Am J Epidemiol.* 1988; 127: 411-414.
- Knoke JD, Gray GC, Garland FC. Testicular Cancer and Persian Gulf War Service. *Epidemiology.* 1998; 9: 648-653.
- Bullman TA, Mahan CM, Kang HK, Page WF. Mortality in US Army Gulf War Veterans Exposed to 1991 Khamisiyah Chemical Munitions Destruction. *AJPH.* 2005; 95: 1382-1388.

**Presentation 15 – Lea Steele**

**Highlights of Recently  
Published Research**

---

Lea Steele, Ph.D.  
September 20, 2005

☆☆ RAC-GWVI

**Recently-published research**

---

- Health effects of Gulf War-related exposures
  - > Human/occupational studies
  - > Animal studies
- Epidemiologic studies of Gulf War veterans
- Multisymptom illnesses: treatments

☆☆ RAC-GWVI

**Health Effects of Gulf War-related Exposures:  
Human studies**

---

Paraoxonase polymorphisms and self-reported ill health in farmers dipping sheep. Povey et al. *Occup Med Jun 2005 55:282*

- > PON1 192 Q form more efficiently hydrolyzes diazinon, sarin than R form; PON1 55 polymorphisms affect PON1 activity levels
- > This study evaluated 409 U.K. farmers: 'cases' had chronic symptoms they attributed to sheep dip, referents did not
- > Homogenous population generated by eliminating subjects with identified diseases or injuries that could explain their symptoms
- > Confirmed previous findings that sheep dippers with chronic symptoms are significantly more likely to carry R allele at position 192 (RR and QR genotypes)
- > Sheep dippers with chronic symptoms also significantly more likely to be LL homozygotes at position 55 (than LM or MM)
- > Support hypothesis that OPs contribute to the chronic ill health of sheep dippers

☆☆ RAC-GWVI

**Health Effects of Gulf War-related Exposures:  
Human Studies**

---

Neurologic symptoms in licensed private pesticide applicators in the agricultural health study. Kamel et al. *Environ Health Perspec Jul 2005 113:877*.

- > High-level pesticide exposure associated with acute, chronic neurological problems; little known about lower-level exposures
- > Agricultural Health Study collected neuro symptom and lifetime exposure information on 18,782 licensed pesticide applicators
- > Number of days of insecticide use was significantly associated with greater number of symptoms, in a dose response fashion
- > Among insecticides, greatest effect from organophosphates, organochlorines
- > Effects persisted after eliminating all individuals with history of pesticide poisoning, excess exposure incident

☆☆ RAC-GWVI

### Effects of Gulf War-related Exposures: Animal Studies

Vaccination alone or in combination with pyridostigmine promotes and prolongs activation of stress-activated kinases induced by stress in the mouse brain. Wang D et al, *J Neurochem May 2005 93: 1010*.

- > Previously reported that variety of stressors induce activation of protein kinases in the brain (immune activation, potential CNS regulation)
- > Immunization with KLH (a vaccine adjuvant) produced modest increase in kinase activation with stress, but prolonged the effect
- > PB alone did not activate kinases, but significantly prolonged kinase activation induced by stress+vaccination, induced marker of neuro injury
- > Concluded that combination of PB, vaccines, and stress act synergistically to produce kinase-mediated brain damage

### Effects of Gulf War-related Exposures: Animal Studies

Pyrethroid pesticide-induced alterations in dopamine transporter functions  
 Elwan et al. *Toxicol Appl Pharmacol Jul 2005 (Epub)*

- > Study found that repeat exposure of mice to pyrethroids increases dopamine uptake mediated by DAT ; longer-term cell exposure results in decrease dopamine uptake, apoptosis
- > Conclude that upregulation of DAT by permethrins may increase the susceptibility of dopamine neurons to toxic insult by other neurotoxins

Neuromechanical effects of pyrethroids, allethrin, cyhalothrin and deltamethrin on the cholinergic processes in rat brain. Hossain et al, *Life Sciences Jul 2005, 77: 795*

- > Previous studies have indicated that pyrethroids differentially modulate acetylcholine release in the brain
- > This study found that pyrethroids significantly increase levels of ACh synthesizing enzyme choline acetyltransferase, and altered uptake of choline
- > Demonstrate mechanisms of pyrethroid effects on cholinergic system

### Epidemiologic Studies Gulf War Veterans

Gulf War Veterans' Health: medical evaluation of a U.S. cohort.  
 Eisen et al, *Ann Intern Med Jun 2005 142: 881*.

- > Clinical evaluations from Phase III of VA's large national study of Gulf War era veterans and their families
- > Clinical evaluations of 1061 Gulf War veterans and 1128 nondeployed era veterans in 16 VAMCs
- > Compared 12 predefined health outcomes in both groups
- > Mean SF-36 PCS was 49.3 for deployed, 50.8 for nondeployed

### Epidemiologic Studies: Gulf War Veterans

	Prev. in Gulf Veterans	Prev. in Non-Gulf	Adj. OR
<i>Fibromyalgia</i>	2.0%	1.2%	2.3*
<i>CFS</i>	1.6%	0.1%	40.6*
<i>Skin conditions</i>	34.6%	26.8%	1.4*
<i>Dyspepsia</i>	9.1%	6.0%	1.9*
<i>Hypertension</i>	9.1%	12.6%	ns
<i>Hepatitis</i>	6.5%	5.2%	ns
<i>Symptomatic arthralgias</i>	6.4%	6.8%	ns
<i>Obstructive lung disease</i>	4.5%	5.9%	ns
<i>Diabetes mellitus</i>	4.2%	3.5%	ns
<i>Peripheral neuropathy</i>	4.8%	5.9%	ns
<i>Hypothyroidism</i>	1.6%	1.2%	ns

\*p<0.05

### Epidemiologic Studies Gulf War Veterans

---

Interpretation of results may vary....

- > Paper concludes: "Ten years after the Gulf War, the physical health of deployed and nondeployed veterans is similar"
- > Presentation of results at IOM meeting also suggested that the health of Gulf veterans similar to nondeployed; Gulf veterans don't have much of a problem
- > Results interpreted by VA scientist as demonstrating a significant, clinically validated problem in Gulf veterans (CFS)

☆☆ RAC-GWVI

### Epidemiologic Studies Gulf War Veterans

---

Major concern re: study approach: Choice of Outcomes

- > Results generally validated results from initial survey, i.e. CFS, skin conditions elevated; hepatitis, diabetes, hypertension not elevated
- > No evaluation of Gulf War-related multisymptom illnesses, consistently-identified primary problem in Gulf War veterans
- > No evaluation of rates of diagnosed conditions thought to be elevated in Gulf War veterans: e.g., migraines, sleep disorders

☆☆ RAC-GWVI

### Epidemiologic Studies Gulf War Veterans

---

Eisen et al, *Ann Intern Med* Jun 2005 142: 881

Summary:

- > CFS, FM, skin conditions, dyspepsia significantly elevated in Gulf War veterans.
- > CFS dramatically increased (OR = 40.6) but affects only 1.6% Gulf War veterans.
- > Physical health summary score similar in Gulf veterans, nondeployed (both ~50)
- > Unclear why study did not address central research questions related to health of Gulf War veterans

☆☆ RAC-GWVI

### Epidemiologic Studies Gulf War Veterans

---

Biological monitoring and surveillance results of Gulf War I veterans exposed to depleted uranium. McDiarmid et al, *Int Arch Occup Environ Health* Aug 2005 [Epub]

- > Reports on physical exams and lab evaluations of 32 Gulf veterans with embedded DU shrapnel, exams provided biannually
- > Fifth of biannual evaluations provided to this cohort (done in 2003)
- > Found that urine uranium continues to be elevated in this cohort 12 years after first exposure
- > Paper concludes that "no clinically significant uranium-related health effects were observed in blood count, blood chemistries, neuropsychological measures, semen quality, or genotoxicity measures."

☆☆ RAC-GWVI

### Epidemiologic Studies Gulf War Veterans

McDiamid et al, *Int Arch Occup Environ Health Aug 2005 [Epub]*

- > Among cohort of 32 veterans, measures were compared between 13 veterans with "high level" urine uranium (>0.10 ug/g creatine) and 19 with lower levels of urinary uranium (<0.10 ug/g creatine)
- > Significant differences reported include:
  - Serum phosphate levels (high)
  - Uranium levels sign assoc with neurocogn accuracy index (intellectual level)
- > Differences approaching significance include:
  - Urine retinol binding protein (high)
  - Neurocognitive accuracy measure (more impairment)
  - Mutation frequencies
- > Low and high U groups had elevated serum prolactin levels

★★★ RAC-GWVI

### Epidemiologic Studies Gulf War Veterans

McDiamid et al, *Int Arch Occup Environ Health Aug 2005 [Epub]*

- Concerns:
  - > Comparisons between "low urine uranium" and "high urine uranium" groups, not between those with/without uranium, or exposed/not exposed
  - > Small sample limits ability to detect significant differences
  - > Differences that are identified are minimized
  - > No information on chronic symptoms, symptom complexes
  - > No information on tumors

★★★ RAC-GWVI

### Multisymptom Illnesses Treatment Studies

Effect of aerobic exercise on patients with primary fibromyalgia. Salek et al, *Mymensingh Med J Jul 2005, 14: 141.*

- 68 adult patients, 2 groups: tricyclic antidepressants+analgesics with/without aerobic exercise
- Treatment 16 weeks; outcomes evaluated include pain severity, # trigger points, sleep regularity, global physician evaluation
- Results: 48% improved with exercise  
39% improved without exercise
- Difference not significant

★★★ RAC-GWVI

### Multisymptom Illnesses Treatment Studies

A randomized clinical trial of an individualized home-based exercise programme for women with fibromyalgia. DaCosta et al, *Rheumatology Jul 2005 [Epub]*

- 79 women with FM, 2 groups: individualized, moderate home-based exercise, usual care
- Treatment 12 weeks; outcomes evaluated FM-specific global health status instrument score, pain intensity score, SCL-90 (psych distress)
- Sign improvement in global health, upper body pain
- No sign differences in lower body pain, psych scores
- Improvements maintained at 3 month and 9 month follow up

★★★ RAC-GWVI

### Multisymptom Illnesses Treatment Studies

---

A randomized controlled trial of dehydroepiandrosterone in postmenopausal women with fibromyalgia. *J Rheumatol* 2005 Jul;1336

- 52 patients with FM, cross-over study
- 3 mos treatment with 50 mg. DHEA (adrenal hormone)
- No significant improvement in pain, fatigue, cognitive function

☆☆ RAC-GWVI

### Multisymptom Illnesses Treatment Studies

---

Pregabalin for the treatment of fibromyalgia syndrome: results of a randomized, double-blind, placebo-controlled trial. Crofford LJ et al, *Arthritis Rheum Apr* 2005, 52:1264.

- 529 patients, 8 week treatment
- Pregabalin (analgesic, antianxiety, anticonvulsant)
- 450 mg/day Pregabalin sign reduced pain scores; sign improvement in sleep measures, fatigue  
29% of treatment grp had  $\geq$ 50% improvement in pain;  
13% placebo

☆☆ RAC-GWVI

### Multisymptom Illnesses Treatment Studies

---

A randomized, double-blind, placebo-controlled trial of pramipexole, a dopamine agonist, in patients with fibromyalgia receiving concomitant medications. Homan et al, *Arthritis Rheum Aug* 2005 52:2495

- 60 patients with FM
- 14 week treatment with pramipexole (dopamine agonist)
- Sign improvements in FM impact score, function, fatigue
- 42% of treatment group had  $\geq$  50% decrease in pain score;  
14% placebo

☆☆ RAC-GWVI

**Presentation 16 – Timothy O’Leary**

	<p><b>VA Tissue Banking</b></p> <p>Timothy J. O’Leary, M.D., Ph.D. Director, BLR&amp;DS Acting Director, CSR&amp;DS</p>

	<p><b>Types of Tissue Bank</b></p>
	<ul style="list-style-type: none"><li>■ Biopsy/autopsy specimens<ul style="list-style-type: none"><li>– May be frozen or paraffin-embedded</li><li>– Quality depends upon many technical factors</li></ul></li><li>■ Serum or blood</li><li>■ Urine</li><li>■ Extracted nucleic acids</li></ul>

	<p><b>What is a Tissue Bank?</b></p>
	<ul style="list-style-type: none"><li>■ Specimens collected and stored for future research purposes that are not specified in the original research protocol are considered “banked specimens.”</li><li>■ Specimens that are collected and retained for diagnostic purposes are not considered “banked specimens” until research use is contemplated.</li></ul>

	<p><b>Examples of VA Tissue Banks</b></p>
	<ul style="list-style-type: none"><li>■ Bronx VA – brain</li><li>■ Denver VA – lung cancer</li><li>■ Iowa city VA – blood for hepatitis C studies</li><li>■ San Francisco – blood for genetic studies of heart disease and mental health</li><li>■ Palo Alto –CNS tissues</li><li>■ West LA – postmortem CNS</li></ul>

### **How many VA Tissue Banks Are There?**

- As of July, 2002 we believe that 53 stations banked tissue, with 18 banking tissue off-site.
- Details are available on only 37 of these sites.

### **Starting a New Repository**

- Demonstrate unmet demand and scientific purpose.
- Meet technical and ethical standards.
- Demonstrate that the cost of operation is appropriate and that it serves a VA purpose.

### **Non-VA Tissue Banks**

- May deposit in NCI Cooperative Oncology Group or NIDA center for Genetics Studies tissue banks without waiver.
- Waiver requires justification:
  - Benefit to veterans
  - Link to clinical data only at VA
  - VA IRB and research committee approval
  - Protocol
  - Informed consent document

### **Sending Research Specimens Outside VA**

- If specimens are sent to a non-VA institution for analysis, such analysis should be outlined in the original research protocol.
- A written agreement must specify the analysis/test to be performed outside the VA.
- The remainder of the specimens must be returned to the original VA for destruction. Alternatively, specimens and related biomaterials may be destroyed at the non-VA institution on condition that the institution certifies, in writing, that the specimens have been destroyed.
- Remaining specimens and/or related biomaterials may not be retained and/or stored by the non-VA institution.

	<b>Clinical Data Considerations</b>
	<ul style="list-style-type: none"><li>■ Clinical and personal data must be maintained under VA control. The clinical information that is shared should not contain any unique identifiers that can be linked to a human subject.</li><li>■ It is imperative that human research subjects donating biological specimens receive the highest level of protection with regard to their linked clinical and personal data.</li></ul>

	<b>Informed Consent Must Specify</b>
	<ul style="list-style-type: none"><li>■ If specimen will be used for future research and must provide a choice for the type of research (research specified in the consent form; research conducted by the PI only; research conducted by other investigators; research related to specific diseases; gene testing, etc.).</li><li>■ If the specimen will be stored without any identifier or if the subject’s identifier and clinical data are linked to the specimen.</li><li>■ If the human subject will be contacted after the completion of the original study.</li><li>■ If the specimens and all links to clinical data are destroyed or removed from the bank upon the subject’s request.</li><li>■ The disposition of the specimen after completion of the study or at the end of the banking period.</li><li>■ Any potential conflict of interest or financial gains for the investigators or the participating institution.</li></ul>

	<b>Communication of Research Results to Clinicians and Human Subjects</b>
	<ul style="list-style-type: none"><li>■ The Clinical Laboratory Improvement Act of 1988 prohibits communication of patient-specific research laboratory results to either subjects or clinicians.</li><li>■ The general research findings should be available to both clinicians and human subjects.</li></ul>

	<b>Other Resources</b>
	<ul style="list-style-type: none"><li>■ NINDS-sponsored brain banks in Parkinson Disease, epilepsy and stroke.</li></ul>

<b>MAVERICK Query</b>	
	<ul style="list-style-type: none"><li>■ “Does the current supply of brain tissue meet the demand by VAHCS research?”</li><li>■ “Evidently, there are few requests to existing VAHCS brain banks by VAHCS research.”</li><li>■ <i>Most requests come from outside VA.</i></li></ul>

<b>Starting a New Bank</b>	
	<ul style="list-style-type: none"><li>■ What is the scientific need?</li><li>■ What are the technical requirements?</li><li>■ Are the specimens available?</li><li>■ What is the cost of obtaining the specimens?</li><li>■ How will specimens be distributed?</li><li>■ What are the policy requirements?</li><li>■ How will tissue bank show worth?</li><li>■ How will policies protect veterans’ interests?</li></ul>

<b>Conclusions</b>	
	<ul style="list-style-type: none"><li>■ VA Tissue Banks support the care of future veterans by facilitating research by today’s veterans.</li><li>■ Must demonstrate that they are needed for high-quality hypothesis-driven research.</li><li>■ Must respect the right of veterans for privacy and autonomy.</li><li>■ Must not unnecessarily duplicate efforts of other federal agencies.</li></ul>

**Presentation 17 – Joel Kupersmith**

## Report of the Office of Research and Development



Joel Kupersmith, MD  
Chief Research and Development Officer  
Office of Research and Development  
Veterans Health Administration  
Department of Veterans Affairs  
September 21, 2005



## VA Research

Our mission is clear and Congressionally-  
mandated :

*“To discover knowledge and create innovations  
that advance the health and care of veterans and  
the nation.”*



## VA Research Standards

- **Is the research based on rigorous science?**
- **Will the research produce data that will drive clinical policy?**
- **Will the research translate to improved health care?**
- **Will the research help veterans?**



## Rich 50 Year History

- **3 Nobel Laureates**
- **6 Lasker Award Winners**
- **Important Discoveries and Inventions**
  - > Devices
    - ✓ Cardiac Pacemaker
    - ✓ Radioimmunoassay
    - ✓ CT Scanner
  - > Treatments
    - ✓ TB
    - ✓ Hypertension
    - ✓ Heart Failure



## Rich 50 Year History

- How your doctor treats you is based in many ways on VA research



## How VA Research Works



## Intramural Research Program

- VA Research is an intramural program.
- Researchers must be employed by VA (5/8s or more in most cases).
- Unlike agencies such as the NIH or DoD, VA has no statutory authority to make research grants to colleges and universities, cities and states, or any other non-VA entity.



## Organization of VA Research

- Four research services with the VA Office of Research and Development (ORD)
  - Biomedical Laboratory R&D Service (BLR&D)
  - Clinical Science R&D Service (CSR&D)
  - Health Services R&D Service (HSR&D)
  - Rehabilitation R&D Service (RR&D)



## Types of Research Sponsored

- Investigator-Initiated Research (Merit Review)
- Mentored Research (Career Development)
- Large-scale, multi-site clinical trials (Cooperative Studies Program)
- Centers of Excellence (all Services)
- Service-Directed Research
- Special Initiatives (e.g., Gulf War Illnesses Research)



## Merit Review

- Merit Review
  - > Our core business
  - > Must produce excellent science
  - > Process must be sacrosanct
  - > Must be absolutely fair (especially in view of history)
  - > Must have uniformity in procedures
  - > New initiative - NIH Impact II Computerized system
    - ✓ Will revolutionize system and also promote uniformity



## Current ORD Leadership

- |                   |                          |
|-------------------|--------------------------|
| ■ CRADO           | Joel Kupersmith          |
| ■ Deputy CRADO    | Vacant                   |
| ■ Director, BLR&D | Timothy O'Leary          |
| ■ Director, CSR&D | Timothy O'Leary (acting) |
| ■ Director, RR&D  | Robert Ruff (acting)     |
| ■ Director, HSR&D | Shirley Meehan (acting)  |



**Long Term Vision**



## Long-Term Vision

- Genomic database
- Integration of research and clinical care



## Long-Term Vision

- Genomic database
  - **Concept:** to link patients' genetic information with the VA electronic health record
  - **Goal:** to develop genetic assessments that will potentially enable "mass customization" of medical treatment
    - ✓ Particularly pharmacogenetic customization



## Genomic Medicine

- **New research will emphasize:**
  - Understanding the role of genetics in the prevention and cause of disease,
  - Using genetic information to improve how clinicians prescribe medications and to prevent adverse reactions,
  - Developing computer systems to effectively and confidentially manage genetic data that can be used to identify genetic predispositions and provide optimal patient care,
  - Developing laboratory capability to do genetic and pharmacogenomic profiling within VA
  - Learning how to use genetic information effectively in everyday practice.



**Integration of Research  
and Clinical care**



**Bed to Bench  
Bench to Bed**



**Bed-to-Bench  
Bench-to-Bed**

- In the VA, research and patient care are under the same roof
- This is unique and we need to take advantage of it
- We need to assure that we are choosing research projects that directly benefit our veterans and that they get the benefits of it



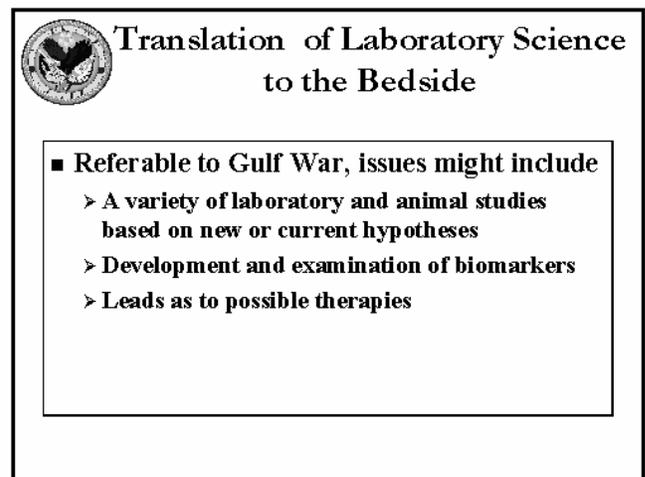
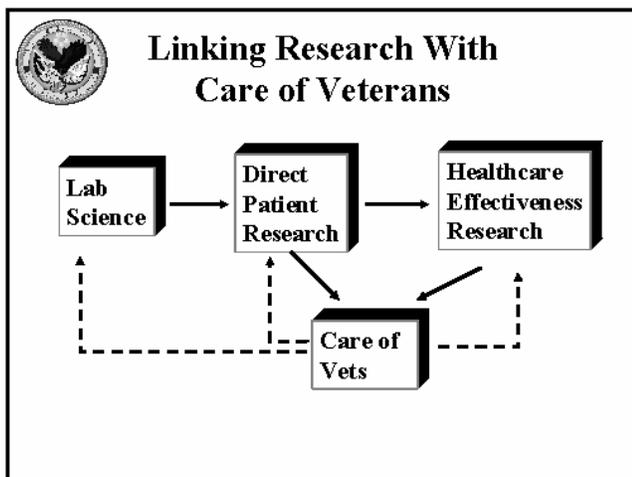
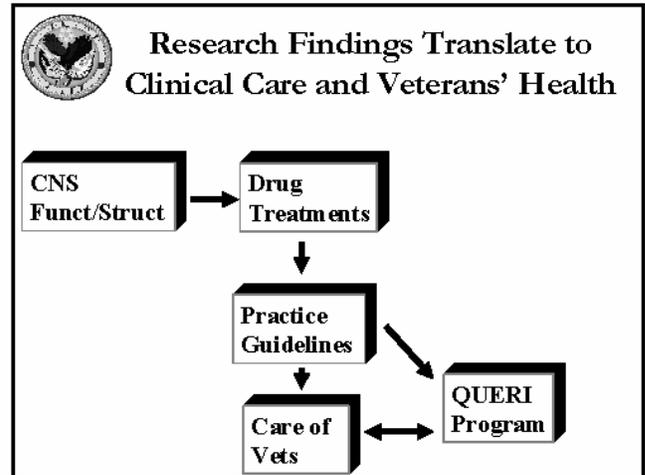
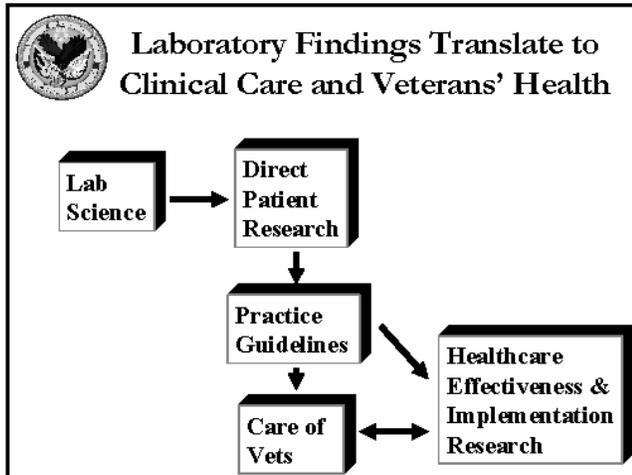
**Bed-to-Bench  
Bench-to-Bed**

- **Bed-to-Bench Bench-to-Bed**
  - Translation of research findings from basic to clinical to health services research
  - Clinical input into research agenda to properly inform it



**Translation of Laboratory Science  
to the Bedside**

- **Steps**
  - Use laboratory science and animal models to develop concepts for clinical care
  - Undertake clinical research based on these concepts
  - Put evidence base concepts into clinical guidelines
  - Assure that guidelines are carried out



**Presentation 18 – William Goldberg**

## Gulf War Update



William J. Goldberg PhD  
Portfolio Manager  
Gulf War  
Veterans Health Administration  
Department of Veterans Affairs



## Gulf War Update

- Topics
  - FY04 RFA
  - FY05 RFA
  - Merit Review process
  - Gulf War portfolio management
  - Some ideas



## FY 2004 RFA



## FY 2004 RFA

- 69 LOIs submitted
- 49 Proposals submitted (~ 71%)
- Review conducted in September 2004
- Funding in FY 2005 (on or after October 1, 2004)



**FY 2005 RFA**



**FY 2005 RFA**

- Areas of interest include studies that have the potential to make significant progress in understanding and treating Gulf War-related conditions
  - > Epidemiologic
  - > Clinical
  - > Laboratory
- Proposals which focus on psychological stress or psychiatric conditions, such as PTSD, will not be considered under this RFA.



**FY 2005 RFA**

- Notification of intent to submit
  - > 67 notifications received
- 44 Proposals submitted (~ 66%)
- Proposals assigned to 1 of 2 Subcommittees
- Review scheduled for Sept. 16 and Sept. 30
- Funding in FY 2006
  - > Review of compliance documentation (IRB, IACUC, etc.) must be completed prior to release of funds
  - > Earliest start date October 1, 2005



**Research Focus of Submitted Proposals**

- Brain and Nervous System Function 15
- Chemical Weapons 2
- Exposures (Non-Infectious) 2
- Pyridostigmine Bromide 6
- Immune Function and Infectious Diseases 5
- Symptoms and General Health 14



### Project Focus of Submitted Proposals

- Diagnosis 9
  - Biomarkers, genomics, etc.
- Exposure 7
  - PB, sarin, particulates, etc.
- Symptoms 22
- Treatment 6
  - massage, IBS, pain, gene therapy



### Merit Review Process

- Notification of intent to submit
- Administrative check of proposals received
- Review and assignment to review panels
  - Evaluation of specific expertise needed for review
- Recruitment of reviewers (2-3 per proposal)
- Written reviews submitted in advance
- Discussion of each proposal at review meeting
- Summary Statement written at meeting



### Review Criteria (written comments and discussion)

- Significance
- Approach
  - Strengths and weaknesses
- Feasibility
- Responsiveness to the RFA
- Relevance to Gulf War veterans' illnesses
- Ethical and safety issues
- Budget



## Gulf War Research Portfolio



## Portfolio Management

- Dr. William J. Goldberg was appointed as portfolio manager in June 2005
  - 7 years experience as Portfolio Manager for Neurological and Sensory Disorders Research Portfolio
  - 15+ Years research experience in ischemia, stroke, spinal cord injury, and brain tumor (glioblastoma) growth and migration
  - Also appointed as the Designated Federal Official for the RAC-WGVI



## FY 2006 Portfolio

- 35 Ongoing projects From 2005 GW Portfolio
  - \$ 10.1 Million
- All projects will be reviewed for continued inclusion in the Gulf War research portfolio
- Projects from the FY 2005 RFA and other solicitations will begin funding on or after October 1, 2005
  - Number and cost will depend on the scientific quality and relevance of submitted proposals to GWVI



## New Initiatives

- Gulf War Treatment Research Center RFA
  - RFA announced in 2006
  - Review of proposals in 2006
  - Funding of approved projects in FY 2006
- Gulf War Merit Review RFA
  - RFA announced in FY 2006
  - Review of proposals in August or September 2006
  - Funding of approved projects to begin on or after October 1, 2006

## Gulf War Update



William J. Goldberg PhD  
Portfolio Manager  
Gulf War Research  
Veterans Health Administration  
Department of Veterans Affairs



### Some Ideas

- Potential mechanisms to expand the portfolio
  - Better communication of RFA announcements
  - Better-focused RFAs
  - One dilemma
    - ✓ Too narrow RFA
      - Not enough applications
    - ✓ To broad RFA
      - Perhaps do not suit purpose



### Portfolio Expansion

- Potential mechanisms to expand the portfolio
  - Partnership with NIH
  - Partnership with pharmaceutical industry
    - ✓ Fibromyalgia
    - ✓ Chronic Fatigue Syndrome
    - ✓ Irritable Bowel Syndrome
  - Partnership with DoD

**Presentation 19 - Han Kang**



**Preliminary Findings**  
**Reported Unexplained Multisymptom Illness Among**  
**Veterans Who Participated in the VA Longitudinal**  
**Health Study of Gulf War Era Veterans**

Meeting of the Research Advisory Committee  
 on Gulf War Veterans' Illnesses  
 September 21, 2005

Han K. Kang, Dr. P.H. and Clare M. Mahan, Ph.D.  
 Environmental Epidemiology Service  
 Department of Veterans Affairs



Unexplained Multisymptom Illness

- Several different symptoms together that persist for 6 months or longer
- Not adequately explained by conventional medical or psychiatric diagnoses
- May be diagnosed as chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, or multiple chemical sensitivity



Presence of Unexplained Multisymptom Illness for 6 Months or Longer

	Gulf		Era	
	Number	%	Number	%
No	3751	65	3104	90
Yes	2016	35	355	10
<b>Total</b>	<b>5767</b>	<b>100</b>	<b>3459</b>	<b>100</b>



Demographic Characteristics of Veterans by Gulf War Deployment and Presence of Multisymptom Illness

Demographics	Gulf MSI %		Era MSI %	
	Yes	No	Yes	No
<b>Gender</b>				
Male	75	82	69	78
Female	25	18	31	22
<b>Race</b>				
White	70	80	77	82
Black	21	14	17	12
Hispanic	6	3	3	3
Others	3	3	3	3
<b>Marital Status</b>				
Married	56	55	60	62
Single	38	40	31	33
Others	6	5	9	5
<b>Median Age (1991)</b>	<b>30</b>	<b>29</b>	<b>33</b>	<b>33</b>

Military Characteristics of Veterans by Gulf War Deployment and Presence of Multisymptom Illness

	Gulf MSI, %		Era MSI, %	
	Yes	No	Yes	No
Rank				
Enlisted	88	81	82	75
Officer	12	19	18	25
Branch				
Air Force	9	15	13	13
Army	73	59	68	65
Marine	9	11	8	9
Navy	9	15	11	13
Component				
Active	34	38	40	39
Guard	32	27	26	27
Reserve	34	35	34	34

Percent Distribution of Veterans by Year First Experienced Unexplained Multisymptom Illness

Year	Gulf	Era
1991 – 1993	67.2	41.4
1994 – 1996	15.0	19.6
1997 – 1999	8.7	18.2
2000 – 2002	7.3	16.9
2003 – 2005	1.9	3.9
Median Year	1992	1995

Effects of Activities on Gulf War Veterans' Unexplained Illness Symptoms

Activity	Effects on Symptoms, %					
	Worse	No effect	Better	Not sure	Not tried	BW*
Light exercise	19.7	38.1	11.9	24.7	5.4	0.6
Vigorous exercise	36.6	21.9	8.0	19.8	13.5	0.2
Smoking tobacco	5.3	21.3	2.0	16.0	55.1	0.4
Drinking alcohol	7.6	28.9	6.5	22.2	34.6	0.9
Maintaining a busy work or social schedule	24.5	38.6	5.1	24.2	7.4	0.2

\* % Better/ % Worse

Effects of Activities on Gulf War Veterans' Unexplained Illness Symptoms

Activity	Effects on Symptoms, %					
	Worse	No effect	Better	Not sure	Not tried	BW*
Maintaining a generally well-balanced diet	1.9	44.7	12.4	30.2	10.6	6.5
Adopting specific eating	2.2	34.7	11.3	26.4	25.2	5.0
Maintaining a regular sleep schedule	5.3	47.0	10.4	26.0	11.1	2.0
Cutting back on work or social activities	4.9	39.9	13.6	24.3	17.1	2.8
Avoiding stressful situations	3.9	36.6	20.0	26.0	13.2	5.0
Avoiding exposure to certain chemicals or smells	4.4	24.4	14.3	27.8	28.8	3.3

\* % Better/ % Worse



**Effects of Activities on Gulf War Era Veterans' Unexplained Illness Symptoms**

Activity	Effects on Symptoms, %					
	Worse	No effect	Better	Not sure	Not tried	B/W*
Light exercise	18.3	38.2	15.8	19.3	8.1	0.9
Vigorous exercise	35.2	21.2	7.5	16.7	19.2	0.2
Smoking tobacco	7.0	17.6	3.2	17.6	54.4	0.4
Drinking alcohol	9.8	25.1	6.8	20.6	37.5	0.7
Maintaining a busy work or social schedule	23.2	33.5	9.0	24.2	13.0	0.4

\* % Better / % Worse



**Effects of Activities on Gulf War Era Veterans' Unexplained Illness Symptoms**

Activity	Effects on Symptoms, %					
	Worse	No effect	Better	Not sure	Not tried	B/W*
Maintaining a generally well-balanced diet.	2.2	36.9	20.4	29.4	10.9	9.1
Adopting specific eating	2.5	29.9	17.8	23.3	26.3	7.1
Maintaining a regular sleep schedule	4.0	42.0	14.7	23.5	15.7	3.7
Cutting back on work or social activities	5.2	34.3	18.3	22.5	19.5	3.5
Avoiding stressful situations	2.9	30.4	25.1	25.9	15.4	8.4
Avoiding exposure to certain chemicals or smells	3.4	23.0	13.6	28.7	31.0	3.9

\* % Better / % Worse



**How Would You Rate the Condition Now?**

Rating	Gulf	Era
Completely recovered	2.3%	5.9%
Much improved	7.3%	12.6%
Somewhat improved	13.9%	22.6%
About the same	35.8%	28.0%
Somewhat worse	25.2%	20.8%
Much worse	15.2%	9.7%



**Category of Treatments that Veterans Have Used for the Unexplained Illness Symptoms**

Treatments	Helped (n)	Made Worse (n)	Ratio**
Prescription Drug	889	175	5.1
Over the Counter Drug	546	62	8.8
Others*	412	135	3.1
Physical Therapy, Surgery	262	85	3.1
Nutrition Supplement and Dieting	207	35	5.9

\*Others include acupuncture, massage, meditation, prayer, relaxation therapy, illegal drug use, cognitive therapy, counseling, interpersonal skills, sleep management, psychotherapy, etc.  
 \*\* A ratio of the number of veterans helped/the number of veterans whose symptoms got worse.

**Top 10 Treatments That Helped Gulf War Veterans' Unexplained Symptoms**

Treatments	Number	Percent
Generic OTC medication	181	7.8
Dieting and Nutritional Supplements	175	7.6
Physical therapy	138	6.0
OTC non-opioid analgesics	131	5.7
Rx antidepressants	126	5.4
OTC non-opioid anti-inflammatories	93	4.0
Rx anti-inflammatory agents	88	3.8
Rx non-opioid analgesics	79	3.4
Physical exercise	69	3.0
Rx stomach acid blockers	62	2.7

**A List of "Other" Treatments That Helped Gulf War Veterans' Unexplained Symptoms**

Treatments	Number	Percent
Acupuncture	5	0.2
Magnets, polarity therapy	6	0.3
Massage	26	1.1
Breathing exercises	10	0.4
Meditation, yoga	10	0.4
Relaxation therapy	50	2.1
Herbal medicine	40	1.7
Illegal drug use	13	0.6
Mental health (counseling, psychologist, psychiatrist)	50	2.1
Radiation therapy	8	0.4
Interpersonal relationship skills	11	0.5
Sleep study	32	1.4

**Effectiveness of Selected Treatments Reported by Gulf War Veterans**

Treatments	N	Improvement, %		Affected Symptoms, %		Top 3 Symptoms Helped
		Short	Long-term	All	Some	
Generic OTC medication	181	72	28	12	88	headache, joint pain, depression
Dieting & Nutritional Supplements	175	53	47	10	90	fatigue, joint pain, IBS
Physical therapy	138	90	10	5	95	joint pain, back pain, muscle pain
OTC non-opioid analgesics	131	91	9	8	92	headache, joint pain, muscle pain
Rx antidepressants	126	52	48	6	94	depression, anxiety, sleep difficulty

**Effectiveness of Non Conventional Treatments Reported by Gulf War Veterans**

Treatments	N	Improvement, %		Affected Symptoms, %		Top 3 Symptoms Helped
		Short	Long-term	All	Some	
Massage	26	80	20	20	80	muscle pain, joint pain, back pain
Meditation, Yoga, Prayer	10	60	40	22	78	anxiety, headache, muscle pain
Relaxation Therapy	50	84	16	15	85	joint pain, fatigue, headache
Herbal Medicine	40	69	31	11	89	memory loss, fatigue, joint pain
Sleep Study	32	69	31	13	87	fatigue, headache, sleep difficulty

### Summary



- A high percentage of Gulf veterans reported having experienced an unexplained multisymptom illness (MSI) than non-Gulf veterans (35% vs. 10%).
- The median year of MSI onset for Gulf veterans was 1992, while the same for non-Gulf Veterans was 1995.
- Exercise, smoking, drinking and maintaining busy schedule, on the whole, made MSI symptoms worse, while maintaining balanced diet, regular sleep, cutting back on work/social activities, and avoiding stressful situations and avoiding exposure to certain chemicals/smells, on the whole, made MSI symptoms better.
- At the time of completing survey, for Gulf veterans, the condition was getting better for 24%, about the same for 36%, and getting worse for 40% of veterans, while the corresponding figures for non-Gulf veterans were 41%, 28%, and 31%, respectively.

### Summary continued



- Prescription drugs and OTC drugs are by far the most common treatments that were used for the MSI symptoms.
- Among the "other" category, treatment by mental health providers (psychologist, psychiatrist, trained counselor), relaxation therapy, herbal medicine, sleep study, and massage, in descending order, were the most common treatments that provided alleviation from the symptoms.
- Top three symptoms that were helped by above treatments included headache, joint/muscle pain, fatigue, depression, anxiety, and sleep difficulty.

**Presentation 20 – Lea Steele**

**RAC Committee Business**

---

September 21, 2005

☆☆ RAC-GWVI

**RAC Committee Business**

---

- Future Meetings, Reports

☆☆ RAC-GWVI

**Next meeting**

---

- Working Meeting
  - > Summarize and compare weight of evidence related to individual war-related exposures and Gulf War illnesses
  - > Discussion of outstanding research questions and priorities
  - > Content of next RAC Report
  - > Additional topics of interest (areas not yet covered?, breaking research, status of VA research programs)

☆☆ RAC-GWVI

**Future Meetings**

---

- Additional Topics
  - > Potential pathophysiological mechanisms underlying GWI; identification of objective indicators, biomarkers
  - > Effects of combinations of exposures
  - > Potentially useful information from comparison groups (Gulf War allies, local populations, nondeployed era veterans)

☆☆ RAC-GWVI

### Next Committee Report

---

#### Early 2006

- Circulate draft 2006 RAC Report for review and comments

### Future RAC Meetings, Report

---

- Questions?
  
- Suggestions?

---

RAC website: [www.va.gov/rac-gwvi](http://www.va.gov/rac-gwvi)

RAC email: [RAC@med.va.gov](mailto:RAC@med.va.gov)

**Appendix B**

**Public Comment 1 – Wesley Crawford**

Wesley CRAWFORD  
~~SSA~~  
Wes - C08904AH00, COM  
352-262-5114

Gentlemen and Ladies of the Committee and attendees my name is Wesley Crawford

I am a honorably discharged veteran who served from 1987 to 1993.

I served in both Desert Shield and Desert Storm. My symptoms from the illness I have are remarkably the same as the veterans you claim that have Desert Storm Illness. At one time or another I have the following symptoms:

Rash on chest ( constant)

Sleeping problems (constant)

Chronic pain from physical activity

Gall stones

Chronic headaches (recently involving mostly the back half of the head but from time to time including the sides and sometimes even the front of the head). Before this illness manifested I used to get migraines once every six months or so. Currently, at present, I have had one migraine in the past 3 years.

I was diagnosed with G6PD upon entering the Navy in boot camp. (see enclosure 1)

My earliest appearing symptoms was the one documented as occurring in 1990 (see enclosure2)

In 1996 I had lymph node in neck swell up to the size of golf ball, hugely deformed. I was informed it was cat scratch by the V.A. I was treated with antibiotics and informed that all biopsies came back negative.(see enclosure 3). A quick side note: In all my years on the internet searching for vets with G6PD, like me, I have only found one. He was in the desert and oddly enough had his lymph node in leg swell in a short time after my neck lymph node and he was told by VA it was cat scratch as well.

Approximately 3 years ago I began having tingling in my arms and legs and radical problems sleeping. The tingling progressed to pain and soon spread to other parts of my body. Since then any physical activity or extended exertion results in pain of increasing intensity. I have learned to regulate my activities accordingly (Attending a chronic pain clinic offered by the VA helped me cope with my new limitations.) My activity level is that of an old man approximately double my age. In addition in 1997 a small break in my hand with no nerve damage resulted in development of what was then termed RSD, affecting my hand. This resulted in loss of right hand flexibility, strength, and range of motion, as well as permanent disfigurement.

Possible exposures causes include :

- 1.Vaccines (mostly likely cause now based on evidence I just recently received)
- 2.Possible exposure at one point to sarin. ( Exposure would have been minute and highly unlikely but can not be ruled out). I am not allowed to disclose any more on this subject although obtaining my ships log records and coordinating them with other records might help determine possible sarin exposure, however it would not have been either of the 2 mentioned and approved sites for sarin exposure. I highly doubt any likely hood of sarin exposure after obtaining copies of my military medical records recently.
- 3.Diesel engine fumes exposure.
4. Additionally, suffered head injury in Navy sporting event that could possibly be contributing to my symptoms

Request/Recommendations:

1. If possible I would like to be examined by any researchers doing research into the vaccine or sarin exposure categories. I realize that a database exists for research and that names are supposedly picked at random, however I cannot wait around for years to never be called for research.
2. I would like to formally request that this research board consider removing the lymph node in my left neck for examination and full and total biopsy by a independent research unit operating from a university rather than a VA hospital.
3. I request that more information about the numbers of troops claiming illness be further separated by branch of military service and the numbers in each branch. With also the numbers further delineated by amount of claims approved and denied for each branch of the military. I request that this information be posted readily on one or all of the desert storm Illness websites operated by the government. If this information is already posted then I simply ask where to find it. The only information I have seen to date shows only the total of all branches combined, not broken down into said categories.
4. I request that you consider asking the DOD to publish the numbers of each branch of veterans that are called for research testing and treatments. As I understand the names for examination for research projects

are pulled totally at random. I am sure that many veterans would be interested in seeing the number of Navy, Army, Marines, Air force and individual reserve units called for research and or testing. I am only asking that numbers be given to each branch and be made readily available to all vets who access the internet. I would also like to see how many of those veterans in each category decline testing or accept research testing.

5. I request that consideration be given to research into results of anthrax vaccine affects on people with blood enzyme disorders. The reason I base my presumption on anthrax vaccine is that G6PD was tested for by Navy as it can result in fatalities or comas if anti malaria drugs are administered. It is possible that newer vaccines such as anthrax can also have lasting effects on people with G6PD. I do not believe I was administered PB but research combing the 2 in people with blood enzyme deficiencies might be needed as well.

6. Considering most the veterans, like myself, have chronic fatigue and or chronic pain it would be nice if your website would allows signs up or contact phone number for contacting someone to reserve speaking time. I called Monday and was bounced around so much on calling in that I finally got tired of the lack of knowledge about this meeting and hung up on the people being rude to me. This was out 5 attempts to reach someone to reserve speaking time.

7. Last but by no means least I would like to formally request that an MRS of my head be administered to me to be compared with other veterans that are confirmed as having this illness. According to the VA my last MRI was normal. If evidence from the MRS suggests anything I request that a new independent MRI be given as well. Again I understand this board adheres to required random testing, however if you lived with this constant pain, sleeping problems, skin problems and more with no definitive answers I am sure you would make any attempt as well to ascertain what is causing your illness.

Closing remarks:

There are Navy veterans as well as other veterans that have this illness that are continuing to be told that they cannot possibly have this illness even with documentation and proof. This illness is not limited to just the veterans that were in the desert during operation Desert Shield/Desert Storm.

Any researchers wishing to contact me can find my name in the Gulf War Illness registry maintained by the DOD.

Last but not least I would like to thank all the people in the VA, independent researchers, and members of this committee that are working hard to help the veterans with this illness. Even though their peers to this day still cling to the old PTSD theory or that only the members of the military in the desert could possibly have this medical illness.

Thank you for your time ladies and gentlemen.

## **Public Comment 2 – Kirt Love**

### **Modeling and Risk Characterization of US Demolition Operations at the Khamisiyah Pit – Veteran interpretation of the data**

OSAGWI / CIA were asked to provide an exposure model related to the March 1991 Khamisiyah demolition. That exposed American troops to the bunkers ammunition contents. HE, Chemical, Biological, etc.

In my presentation to the RAC on September 20<sup>th</sup> 2005 I provided a crude PowerPoint of some of my RAW data on the interpretation of this information.

Information consisted of:

- Current Digital Elevation Models of Iraqis terrain features
- DEM of Iraqi irrigation /drainage features of Iraq
- CHPPM Oil Well Fire Plume model image
- CIA imagery of pit smoke scarring
- Soviet Topographical map of direction of airfields surrounding the Pit
- DEM mapped over NASA MODIS satellite images showing Shamal winds
- CIA Mar 11 satellite image of Iraq smoke plumes
- Shifted Bunker demolition plume image over NASA MODIS image
- Three different models of demolition data (OSAGWI, CIA)

My discussion was over the one particular day, March 10<sup>th</sup> 1991.

In the Government model the data shows a plume boundary that is closest to matching weather patterns of this region. But, with a minor twist. The model shows the winds carrying the plume more of a north to south flow, then curling back into Saudi Arabia.

Prevailing winds of Iraq follow the valley terrain under the Iranian mountains to the Persian Gulf. Of ten called the Shamal winds, they blow in a continuous pattern year round.

Soviet Topographical map of this region shows the surrounding air fields are built into the wind for take off. Which is from South East to North West in line with the valley contours of the mountains.

DEM images establish that the terrain curves around the Iranian mountain region toward the Persian Gulf. The DEM irrigation / drainage images show the elevation or Iraq tapers toward the river system in the valley as it flows out the Persian Gulf.

CHPPM modeling data of the Oil Well Fire smoke plumes also support the winds in March 1991 flowing out into the Persian Gulf.

A recent 29 days of sequential NASA MODIS imagery of Iraq shows Shamal wind direction in this region. 26 out of 29 days the winds followed there normal course. 2 days they reversed, and one day was North to South. 89% of the time the winds flowed toward the Persian Gulf from the Khamisiyah Pit location.

CIA imagery of the smoke scarring around the Pit shows a more of a Easterly wind pattern in the lighter parts of the ground shadows.

A March 11<sup>th</sup> 1991 CIA image of Kuwait shows the wind flows in the opposite direction of its CIA A-66 wind direction model for that day. Based on Oil Well fire plume trailing out into Persian Gulf from Kuwait.

To this day Deployment Health Support Directorate has refused to put up detailed Satellite images of Kuwait during March 10<sup>th</sup> through March 13<sup>th</sup> 1991 in its Khamisiyah report. Which with the burning oil wells would show wind patterns for each day in question.

GAO produced a 41 page report GAO-03-833T on this. But, the report failed to produce detailed satellite imagery for those days. They were influenced to put their resources instead into the Lawrence Livermore medic models, which offered equally as vague data in its conclusions.

Visual data contradicts COAMPS prepared by NRL in the Pit modeling.

When you take the DOD modeling image for March 10<sup>th</sup> 1991, and overlay it on the NASA MODIS image for Iraq, then shift to match normal wind directions for this region you see a slight change. The plume now engulfs most of 1<sup>st</sup> and 3<sup>rd</sup> AD, VII Corp, and then flows down in Kuwait City. Which would mean the plume crossed over more than 350,000 to 400,000 troops in this region.

75% of CIA's wind modeling (A-61 to A-72) goes completely against the normal wind patterns in southern Iraq. Only A-62 comes close to following the Shamal wind patterns.

It is my foregone conclusion that DOD deliberately modeled the data to pass between major troop positions to avoid liability. To reduce the number of claims filed, and troops notified to a minimum. Rather than admit the plume possibly covered around 60% of the troops in theater.

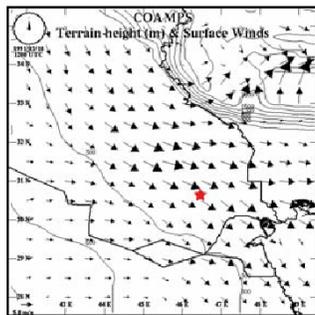
These are only attachment notes to the RAW data shared with the RAC. Final notes and my report will be available in 2006 once I procure the high altitude weather data from the March 1991 demolition in Iraq. Then I can complete my own multi layer vector analysis based on current DEM information on Iraq.

One minor correction from the meeting, I had mislabeled CIA March 11<sup>th</sup> image as March 10<sup>th</sup>. Was in a rush to produce powerpoint. But, in the below attachments you see the CIA satellite image totally contradicts the A-66 CIA wind model for that day.

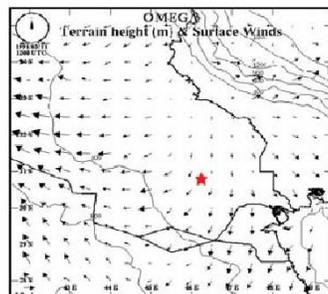
Thank you for your time.

Sincerely  
Kirt P. Love  
Director, DSBR

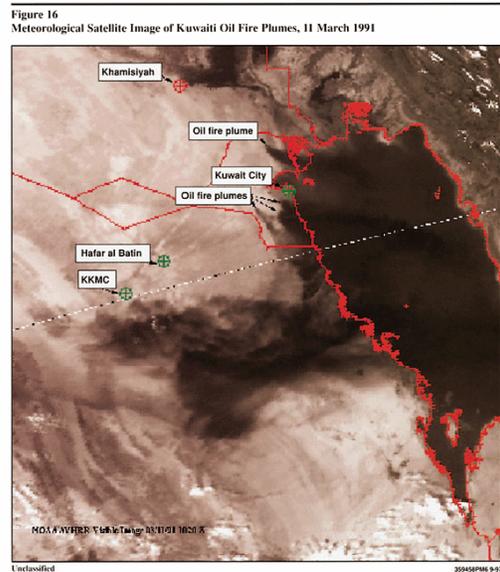
COAMPS modeled wind fields, Mar 10, 1991.  
Fig A-62, OSAGWI, Technical Report: Modeling and Risk  
Characterization of US Demolition Operations at the  
Khamisiyah Pit, Apr 16, 2002



OMEGA modeled wind fields, Mar 11, 1991.  
Fig A-66, OSAGWI, Technical Report: Modeling and Risk  
Characterization of US Demolition Operations at the  
Khamisiyah Pit, Apr 16, 2002



Satellite Image of Oil Fire Plumes, Mar 11, 1991.  
Fig 16, CIA, Modeling the Chemical Warfare  
Agent Release at the Khamisiyah Pit, Sep 4, 1997.



**Appendix C**

**Document 1 – Overview of FY2005 VA Funding for Gulf War Research**

**Overview of FY2005 VA Funding for Gulf War Research**  
*(summarized from information provided by Dr. Kupersmith 9/13/05)*

VA’s Office of Research and Development has provided information to the Committee indicating that just over 9 million dollars was allocated for Gulf War Research projects in FY2005. The two major questions addressed below are: 1) When were these projects initially funded? and 2) What types of projects were funded? Additional information is provided on funding provided for ALS and lung cancer research in FY2005.

**When were FY2005 Gulf War Research projects initially funded?**

<b>Total FY2005 Gulf War Research Funding/ By Funding Period</b>		
Total Funding for Gulf War Research in FY2005	\$ 9,125,736	(100%)
Projects funded prior to FY2005	\$5,336,188	(58%)
Projects funded in response to FY2004 RFA	\$2,074,741	(23%)
Additional projects funded in FY2005	\$1,714,807	(19%)

The majority of the FY2005 Gulf War Research funding (58%) was for projects funded prior to FY2005, as indicated above. About \$3.8 million was allocated in FY2005 for previously unfunded research, of which over half was for projects submitted in response to the special April, 2004, Gulf War Illness RFA. Thus, only \$1.7 million (19%) of the \$9.1 million funding identified as being allocated for Gulf War Research in FY2005 was for projects newly-approved and funded in FY2005.

**What types of projects were funded? Research Newly-Approved and Funded in FY2005**

<b>Gulf War Research Projects Newly-Approved and Funded in FY2005/ By Research Topic</b>		
Total Funding for Newly-Approved and Funded Gulf War Research in FY2005	\$1,714,807	(100%)
ALS research (not Gulf War-specific)	\$ 819,216	(48%)
Projects with no clear relevance to the health of Gulf War veterans	\$ 476,620	(28%)
Projects related to multisymptom illnesses, Gulf War exposures	\$ 418,971	(24%)

As shown, of the \$1.7 million allocated for Gulf War Research projects that were newly-approved and funded in FY2005, nearly half (48%) was for ALS research and 28% was for projects unrelated to the health of Gulf War veterans. The remainder (\$418,971, or 24%) was allocated for projects related to Gulf War veterans’ multisymptom illnesses or the effects of Gulf War-related exposures. However, review of specific projects in this category indicates that most of this “new” funding (\$322,532) was provided to Dr. Weiner’s group at the San Francisco VAMC, for continuation of ongoing neuroimaging studies of Gulf War veterans. The remainder (\$96,439) was provided for secondary analysis of data collected in VA’s earlier clinical study of Gulf War-era veterans. This means that, depending on interpretation, either \$96,439, or no funding has been provided for new research projects specific to Gulf War veterans in FY2005.

**What types of projects were funded? Total FY2005 Research Funded in FY2005**

<b>Total FY2005 Gulf War Research Funding /By Research Topic</b>		
Total Funding for Gulf War Research in FY2005	\$ 9,125,736	(100%)
Projects related to multisymptom illnesses, Gulf War exposures	\$2,313,107	(25%)
Other projects specific to health of Gulf War veterans	\$ 209,897	(2%)
ALS research (not Gulf War-specific)	\$2,965,541	(32%)
Projects related to effects of psychological stress and psych illness	\$1,620,683	(18%)
Projects with no clear relevance to the health of Gulf War veterans	\$2,016,508	(22%)

The table above provides summary information on total funds allocated for GWI research in FY2005—including new and ongoing projects. Overall, about 2.3 million of the 9.1 million dollar total (25%) allocated for Gulf War Research in FY2005 was for projects that focused on the multisymptom illnesses affecting Gulf War veterans, or on effects of Gulf War-related exposures. Additional FY2005 funding included \$209,897 (2%) provided for other projects specifically relevant to the health of Gulf War veterans, nearly \$3 million (32%) for ALS research not specific to Gulf War veterans, about \$1.6 million (18%) for studies related to effects of psychological stress, and over \$2 million (22%) for projects that have no clear relevance to Gulf War veterans or Gulf War illnesses.

**Information on Funding for ALS, Lung Cancer, and Restoring Function after Limb Loss**

All ALS research funded after July, 2004, is identified as “Gulf War Research”. None of the funded ALS projects identified appear to be Gulf War-specific, or studies limited to Gulf War veterans. ALS research represents the largest category of “Gulf War” research funded in FY2005.

In addition, the FY2005 “Gulf War Research” category includes two previously-funded lung cancer research projects totaling \$462,746. Rates of respiratory illness and cancer have both been evaluated in Gulf War veterans, and there has been no indication that lung cancer disproportionately affects this group. Therefore, the lung cancer studies identified can not reasonably be considered Gulf War research.

The single “Gulf War” research study receiving the largest amount of funding (\$1.3 million) in FY2005 is a project that will focus on restoration of function after limb loss. Although this issue has been a problem in Operations Iraqi Freedom and Enduring Freedom, it is not relevant to the health issues associated with the 1990-1991 Gulf War.

**FY2005 ORD Support for Gulf War Research**

**Document 2 – Gulf War Research Projects FY2005 – by Topic and Period Funded**

VAMC	Full Name	Title	Start	Total FY 2005*	Period Funded		Relevance to Gulf War Illnesses, Exposures								
					Prior to 04 RFA	Funded under FY04 GWI RFA	Funded in 05, other	Gulf War multisym illness, effects of exposures	ALS, Gulf War	ALS, General	Other, relevant to health of Gulf Vets	Stress and Psych illness	No clear relevance to Gulf War illnesses		
Baltimore, MD	Fishman, Paul S. (M.D., Ph.D.)	Mechanisms of Neuronal Degeneration	07/01/99	\$ 56,200	X				\$ 56,200						
Boston, MA	White, Roberta F. (Ph.D.)	Boston DVAMC Environmental Hazards Center, Behavioral Neurotoxicology	04/01/00	\$ 337,200	X				\$ 337,200						
Durham, NC	Oddone, Eugene Z. (M.D.) Lavori, Philip (Ph.D.) Kasarskis, Edward J. (M.D., Ph.D.)	National Registry of Veterans with ALS	07/01/02	\$ 682,187	X					\$ 682,187					
East Orange, NJ	Servatius, Richard J. (Ph.D.)	Neurochemical and Neurobehavioral impact of Pyridostigmine Bromide Treatment and Stress	10/01/02	\$ 248,458	X								\$ 248,458		
New Orleans, LA	Vasterling, Jennifer J. (Ph.D.)	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel	01/01/03	\$125,428	X							\$125,428			
Durham, NC	Madison, Roger (Ph.D.)	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness	04/01/03	\$ 281,000	X				\$ 281,000						
Bronx, NY	Golier, Julia (M.D.)	HPA-AXIS Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans	10/01/03	\$ 163,205	X								\$ 163,205		
East Orange, NJ	Huang, Hosea F.S. (Ph.D.) Ottenweller, John E. (Ph.D.)	Pituitary Adrenal Function in People with Fatiguing illness	10/01/03	\$ 276,112	X				\$ 276,112						

\* Includes 12.4% administrative overhead

FY2005 ORD Support for Gulf War Research

VAMC	Full Name	Title	Start	Total FY 2005*	Period Funded			Relevance to Gulf War Illnesses, Exposures							
					Prior to 04 RFA	Funded under FY04 GWI RFA	Funded in 05, other	Gulf War multitym illness, effects of exposures	ALS, Gulf War	ALS, General	Other, relevant to health of Gulf Vets	Stress and Psych Illness	No clear relevance to Gulf War illnesses		
Durham, NC	Wilson, Wilkie A. (Ph.D.)	The Role of Dietary Choline in Neuroprotection	07/01/04	\$ 326,604	X			\$ 326,604							
East Orange, NJ	Cook, Dane B. (Ph.D.)	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	07/01/04	\$ 128,698	X			\$ 128,698							
West Los Angeles, CA	Reckamp, Karen L. (M.D.)	Translational Research of dendritic cell-based therapies in lung cancer	07/01/04	\$ 239,420	X									\$ 239,420	
Providence, RI	Aaron, Roy (M.D.)	Rebuilding, Regenerating and Restoring Function after Limb Loss	08/01/04	\$ 1,300,468	X									\$ 1,300,468	
Bedford, MA	Ferrante, Robert J. (Ph.D.)	National VA Amyotrophic Lateral Sclerosis Research Consortium	09/15/04	\$ 1,171,208	X					\$ 1,171,208					
Ann Arbor, MI	Fink, John K. (M.D.)	Novel Cause of Motor Neuron Disease	10/01/04	\$ 166,352			X			\$ 166,352					
Baltimore, MD	Yarowsky, Paul J. (Ph.D.)	MR Tracking of Stem Cells for Replacement Therapy in ALS	10/01/04	\$ 236,730		X				\$ 236,730					
Boston, MA	White, Roberta F. (Ph.D.)	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans	10/01/04	\$ 159,552		X			\$ 159,552						
Bronx, NY	Yehuda, Rachel (Ph.D.)	Glucocorticoid Responsivity in Gulf War Veterans	10/01/04	\$ 168,600		X							\$ 168,600		
Denver, CO	Winn, Robert A. (M.D.)	Role of WNT signaling pathway in Lung Cancer	10/01/04	\$ 223,326			X							\$ 223,326	
East Orange, NJ	Beck, Kevin (Ph.D.)	Interceptive Stressor Conditioning: A Model for Gulf War Illness	10/01/04	\$ 193,440		X							\$ 193,440		
East Orange, NJ	Weaver, Shelley A. (Ph.D.)	Interactions Between Maternal Care, Stress and Pyrostigmine Bromide	10/01/04	\$ 60,134		X							\$ 60,134		

\* Includes 12.4% administrative overhead



FY2005 ORD Support for Gulf War Research

VAMC	Full Name	Title	Start	Total FY 2005*	Period Funded		Relevance to Gulf War Illnesses, Exposures								
					Prior to FY04 RFA	Funded under FY04 GWI RFA	Funded in 05, other	Gulf War multysym illness, effects of exposures	ALS, Gulf War	ALS, General	Other, relevant to health of Gulf Vets	Stress and Psych Illness	No clear relevance to Gulf War illnesses		
San Antonio, TX	Richardson, Arlan G. (Ph.D.)	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders	04/01/05	\$ 295,938		X		\$ 295,938							
San Antonio, TX	Van Remmen, Holly (Ph.D.)	Role of Mitochondrial Oxidative Stress in ALS	04/01/05	\$ 55,188		X		\$ 55,188							
Tampa, FL	Patel, Niketa A. (Ph.D.)	Alternative Splicing in Human NT2 Cells	07/01/05	\$ 49,737		X							\$ 49,737		
Washington, DC	Kang, Han K. (Dr. P.H.)	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries	07/01/05	\$ 42,206	X					\$ 42,206					
Washington, DC	Kang, Han K. (Dr. P.H.)	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004	07/01/05	\$ 42,262	X					\$ 42,262					
<b>Total FY 2005 funding</b>				<b>\$ 9,125,736</b>				<b>\$ 2,313,107</b>	<b>\$ -</b>	<b>\$ 2,965,541</b>	<b>\$ 209,897</b>	<b>\$ 1,620,683</b>	<b>\$ 2,016,508</b>		
<b>Amount funded prior to FY2005</b>				<b>\$ 5,336,188</b>				<b>\$ 1,349,614</b>	<b>\$ 1,909,595</b>	<b>\$ 125,428</b>	<b>\$ 411,663</b>	<b>\$ 1,539,888</b>			
<b>Amount newly funded in FY2005</b>				<b>\$ 3,789,548</b>				<b>\$ 963,493</b>	<b>\$ -</b>	<b>\$ 1,055,946</b>	<b>\$ 84,469</b>	<b>\$ 1,209,020</b>	<b>\$ 476,620</b>		
<b>Funded in FY2005 under FY2004 RFA</b>				<b>\$ 2,074,741</b>				<b>\$ 544,522</b>	<b>\$ -</b>	<b>\$ 236,730</b>	<b>\$ 84,469</b>	<b>\$ 1,209,020</b>	<b>\$ -</b>		
<b>FY2005 funding other than FY04 RFA</b>				<b>\$ 1,714,807</b>				<b>\$ 418,971</b>	<b>\$ 819,216</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 476,620</b>	<b>\$ -</b>		

\* Includes 12.4% administrative overhead

**Appendix D**

**September 30, 2005 Letter from Committee to Secretary Nicholson**



**Research Advisory Committee on Gulf War Veterans' Illnesses**

September 30, 2005

The Honorable R. James Nicholson  
Secretary of Veterans Affairs

Dear Mr. Secretary:

The Committee deeply appreciates your making time in your busy schedule to participate in our meeting last week. We have learned from experience that the active interest of the Secretary of Veterans Affairs is indispensable to our mission, and we are extremely grateful for your personal support.

We also welcome the participation of Dr. Kupersmith, Dr. O'Leary, and Dr. Goldberg. Their comments on how to build a viable Gulf War Illnesses (GWI) research program were constructive, and we look forward to working with them. The Committee wishes to commend the performance of Dr. Kang, whose study is referenced below, as an example of dedication among individual VA scientists in the field. Dr. Kang delayed his study by several months in order to incorporate questions suggested by the Committee regarding ill veterans' experience with treatments.

As your advisors, however, we are obliged to point out that the recent actions of the Department of Veterans Affairs with respect to GWI research present a very different picture.

The public commitment by the former Secretary of Veterans Affairs to fund up to \$15 million in new research in FY2005 has been disregarded. The Office of Research and Development has no plans to recover this lost year. ORD is padding GWI research totals by lumping in research initiated in previous years, general research on ALS, and additional topics not related to GWI.

The VA Environmental Agents Service has launched several misguided studies by the Institute of Medicine. When proposed, these studies were not reviewed by the Research Advisory Committee, as required by statute. By restricting the questions asked and/or the research to be considered, these studies have been designed to invite results that imply Gulf War illnesses are no different from the expected health consequences of any war.

Appointments to the new GWI merit review board, created by former Secretary Principi to ensure that proposed GWI studies were evaluated by scientists familiar with GWI research and related topics, have predominantly included VA researchers and other scientists with limited expertise in this area – perpetuating the situation the board was created to solve.

Meanwhile, VA field researchers describe the magnitude of the problem. Following your appearance Wednesday morning, Dr. Han Kang, director of the VA Environmental Epidemiology Service, reported the latest results from VA's ongoing major survey of Gulf War veterans and non-deployed veterans of the same era. The results show that fully 25 percent of Gulf veterans have chronic multisymptom illness over and above the background rate found in their non-deployed counterparts. This finding confirms the numbers of ill veterans indicated by earlier studies and highlighted in this Committee's 2004 Report.

In summary, the problems in VA Gulf War illnesses research management have only begun to be addressed. These problems reflect a lack of staff commitment observed over the course of the past three and a half years the Committee has been in existence. These problems need to be resolved before meaningful progress can be made in improving the health of ill veterans.

Very respectfully,

James Binns, chairman  
Beatrice A. Golomb, MD, PhD  
Joel C. Graves  
Robert W. Haley, MD  
Marguerite L. Knox, MN, NP  
William J. Meggs, MD, PhD  
Stephen L. Robinson  
Steve Smithson  
Lea Steele, PhD

Jack Melling, PhD, consultant